MITRAL STENOSIS

A FOLLOW UP OF 351 PATIENTS

By

Knud Henning Olesen



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Preface

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Knud Henning Olesen

Contents

Chapter V

Chapter VI

Introduction

The purpose of the present book is to afford a contribution to the description of the *course and prognosis of mitral stenosis*

I was inspired to take up this work by the dilemma of today s cardiologist when he has to decide whether or not a heart operation is advisable for a patient with mitral stenosis

The remarkable progress in the field of surgery of the heart has caused the performance of mitral valvulotomy without prohibitive risk and with the prospect of a good preliminary result to be a reality today Even though the long term effect of mitral valvulotomy cannot yet be estimated the pre liminary results of the operations have been so encouraging that the present day cardiologist has to consider to an increasing extent the advisability of this operation

Owing to this situation it is considered advisable to revise the experience of the spontaneous course of mitral stenosis given in the literature and to afford a new contribution to this

The present work is a clinical investigation based upon a series of 351 patients with mitral disease collected from a hospital department and from a specialist practice It took the form of clearing up the subsequent fates of these patients and comprises a follow up examination of those who survived after a period from 3 to 20 years

A brief survey of the historical development of the recognition diagnosis and pathology of mitral stenosis is first given Mention is then made of pre vious investigations into the course and prognosis of the disease This is fol lowed by a description of the series of cases upon which the work is based of its classification of the procedure in dealing with the material and of the results of the writer s investigations

CHAPTER I

Diagnosis Aetiology and Pathophysiology of Mitral Stenosis

HISTORICAL DEVELOPMENT

The earliest observations of mitral stenosis were made by the patho anatomists more than 100 years before the clinical diagnosis was possible

The first clear and exhaustive description of mitral stenosis was given by *Vieussens* in 1715 in his textbook with a famous drawing by Simonneau *Morgagni* too described mitral stenosis in 1761 under the title of ossification of the mitral valve

The clinical diagnosis of mitral stenosis did not become possible until in the nineteenth century

The first description of the diastolic thrill at the apex was given by *Corvisart* (1806) The presence of the thrill was confirmed by *Laennec* who pointed out that the thrill corresponded to what he owing to his erroneous interpretation of the heart revolution called a systolic murmur at the apex (*Laennec* 1819)

The auscultatory criteria of the diagnosis of mitral stenosis were established about the middle of the last century by *Hope* in England (1840) by *Barth and Roger* (1844) and by *Fauvel* (1843) in France and *Skoda* in Vienna (1854)

This epoch has been illustrated also by Scandinavian authors e g in a clear and concentrated thesis by the Finnish author *C Steven* of 1847 and by the Dane *C E With* in his thesis on the differential diagnosis of valvular disease in the heart of 1858 (*With* 1858) which clearly reflects the discussions of the period

Duroziez s publications of 1862 and 1877 ended this period they gave a very lucid description of the auscultatory picture of mitral stenosis as interpreted at this time

The following findings were especially emphasized by *Duroziez* (1) A thrill *at the apex corresponding to the rumbling diastolic murmur* (2) *accentuation* of the 1st sound which is of great importance to the diagnosis of pure mitral stenosis as the accentuation is absent in the presence of the systolic apical murmur indicating a simultaneous mitral incompetence (3) frequent splitting

of the 2nd sound which may be loudest at the apex or at the sternum (4) a rasping rumbling or wheezing presystolic murmur at the apex which ofter fuses with the diastolic murmur and disappears when the pulse rate become irregular (5) the very frequent diastolic rumbling murmur at the apex which is of variable duration and often fuses with the split 2nd sound or with the presystolic murmur

The occurrence of the sounds and murmurs is explained thus by *Duro ie* (1) The accentuated 1st sound is caused partly by the closure of the mitral valves though it is possibly mostly due to the closure of the tricuspid valves as the right ventricle is generally situated anteriorly closest to the thoracic wall (2) the split 2nd sound is due to the closure of the aortic and pulmonary valves which does not take place exactly at the same time (3) the presystolic murmur is due partly to the auricular systole partly to the first part of the ventricular systole and (4) the diastolic murmur is caused by the diastolic filling of the left ventricle through the narrowed mitral valve

It will appear from this extract from the works of *Duro ie* that posterity has had very little to add to the safety of the diagnosis of mitral stenosis obtained already then and to the explanation of the origin of the murmurs Actually it is only the split 2nd sound which has later become the subject for a different evaluation *Sansom* (1881) described the *reduplication of the second sound* in mitral stenosis and considered that the sound was due to a sudden stretching of the mitral valves when the blood from the left atrium passed into the ventricle between the wall of the latter and the parietal surface of the valves *Rouches* (1888) and *Potain* (1894) distinguished between a *dédoublement* of the 2nd sound with a maximum at the upper precordium and *claquement d'ouverture de la mitrale* which has a maximum at the apex These authors considered that the changed mitral valves soon after opening at the beginning of the diastole would stop their movement owing to the pathological changes would be stretched and give rise to *un bruit net bref claquant*

Phonocardiographic studies have confirmed the previous findings that there may in mitral stenosis occur both a reduplication of the 2nd sound at the upper precordium which cannot be distinguished from the physiological re duplication and farther down over the precordium a three stroke rhythm which can be heard and recorded in more than half the number of cases examined and is now an important aid in the diagnosis of mitral stenosis (*Margolies and Wolferth* 1932 *Lian et al* 1941)

The extra sound which in French literature is termed *claquement d ouverture de la mitrale* in English literature *opening snap of the mitral valve* often referred to in Danish as Mitralklikket (the *mitral snap*) (*Warburg* 1913) is characterized by its being a sharp dry snap different from the 2nd sound in contrast with the split 2nd sound with two almost identical components As a rule the intensity of the mitral nap is greatest within the apex at the sternal

end of the fourth intercostal space to the right of and above the point where the diastolic murmur is most distinctly heard The interval between the components of the reduplicated 2nd sound is generally under 0 03 second whereas the interval from the beginning of the 2nd sound to that of the extra sounds generally varies from 0 06 to 0 11 second (*Margolies and Wolferth* 1932) *Lian et al* (1941) state the interval to be from 0 08 to 0 09 second

When the mentioned modification of the interpretation of the split 2nd sound is considered and when it is stressed that an accentuation of the 2nd pulmonary sound is today considered part of the fully developed auscultatory picture of mitral stenosis *Duroziez's* stethoscopical criteria for the diagnosis of the isolated mitral stenosis established in the last century can otherwise be fully accepted today It may be added here that the characteristic diastolic or presystolic murmurs can in some cases be heard only when auscultation takes place with the patient in the left recumbent position or after exertion

Already *Duroziez* considered that a *systolic murmur at the apex* in the presence of the mentioned classic signs of mitral stenosis suggested the simultaneous presence of mitral incompetence he also stressed that the accentuated first sound would then lose its characteristic stamp Furthermore it was emphasized by *Duroziez* that the systolic murmur may sometimes disappear and that the estimate of the mitral incompetence may therefore be doubtful (*Duroziez* 1862 and 1877)

This view that a distinct systolic murmur at the apex in the presence of the classic auscultatory findings in mitral stenosis suggests that the mitral stenosis is combined with some degree of mitral incompetence has since been widely accepted (*White* 1944 *Friedberg* 1950 *Vaquez* 1928 *Mouquin* 1933) It is quite evident from post mortem studies that mitral stenosis must very often be accompanied by some degree of incompetence because the stiff and immovable cusps are unable to close the mitral orifice during the systole It is easy to ascertain the presence of mitral stenosis at autopsy and the safety of the clinical diagnosis according to the criteria mentioned has been very great The pathologic anatomical estimate of the degree of mitral incompetence in the presence of mitral stenosis is however somewhat more difficult

For many years before the surgical treatment of mitral stenosis was introduced it had become the custom of many clinicians to consider the mitral stenosis as the main trouble in mitral valvular disease consequently the concomitant incompetence in mitral stenosis received very little attention during that period The clinical criteria for diagnosing mitral incompetence in the presence of clinical mitral stenosis had therefore not been further elaborated

With the introduction of *mitral valvulotomy* in the treatment of mitral stenosis a new situation arose The clinician now had to decide whether the patient suffered from a preponderant mitral stenosis or from a preponderant

mitral incompetence as the former could probably be relieved by mitral valvulotomy whereas the latter should not be operated on

Mitral valvulotomy in itself proved to afford valuable information on the problem of mitral stenosis and mitral incompetence as it became possible during the operation to *estimate in vivo the function of the diseased mitral valve* With a finger in the left atrium the heart surgeon is able to estimate the degree of mitral stenosis during the diastole and during the systole he can feel the degree of regurgitation through the mitral ostium The regurgitation is felt as a jet the intensity of which indicates the degree of backward flow A slight degree of regurgitation is best felt with a naked finger introduced into the atrium (*Husfeldt* 1953) It should of course be borne in mind that the surgical estimate of the mitral valve function is made under circumstances which may convey a wrong impression of the patient s usual valvular function as a low blood pressure and an increased heart rate may reduce the regurgitation or a loss of blood from the left atrium may increase the regurgitation at the moment of palpation also that the result of the estimate will be highly dependent on the surgeon s experience but nevertheless there can be no doubt that this method of examination used *in vivo* is much superior to the pathologic anatomical estimate of the function of the mitral valve

The existing series of cases in which the classic stethoscopical criteria for the mitral disease diagnoses have been compared with the surgical estimate of the function of the mitral valve *in vivo* all show the same tendency Patients with a characteristic diastolic and/or presystolic apical murmur and absent systolic murmur will almost always have a practically pure mitral stenosis In a series from the University Hospital Copenhagen operated on by *Husfeldt and coworkers* the writer thus counted 29 out of 34 patients of this group (85 per cent) whereas 5 patients had a tight to moderate stenosis with slight to moderate regurgitation (15 per cent) No case of preponderant or pure regurgitation occurred in this group Several series in the literature show similar experiences and pure mitral regurgitation without stenosis has very seldom been found in this group (*Abelmann et al* 1953 *Venner and Holling* 1953 *Gorlin et al* 195? *Soulie et al* 1952 *Janton et al* 1952)

Among patients who in addition to the characteristic diastolic presystolic apical murmur had a systolic murmur at the apex the aforementioned series from the University Hospital Copenhagen showed in 5 out of 16 cases (one third) a practically pure mitral stenosis in 6 cases (one third) a tight to moderate stenosis with slight to moderate regurgitation whereas 5 cases (one third) showed predominant regurgitation with slight stenosis All cases of this series thus presented some degree of mitral stenosis one third being estimated as cases of predominant regurgitation (or incompetence) The cases with predominant incompetence showed the highest frequency of loud systolic murmurs

although faint systolic murmurs were also represented in this group These experiences are in accord with the findings of *Abelmann et al Venner and Holling* and of *Burchell and Edwards* (1953)

Experience thus shows that the criteria for the clinical diagnosis of isolated mitral stenosis established by *Duroziez* and his contemporaries are broadly speaking undisputed and therefore applicable today Patients with a charac teristic diastolic and/or presystolic apical murmur and absent systolic murmur will in the majority of cases present a practically pure mitral stenosis Patients who in addition to the diastolic presystolic murmur have a systolic apical murmur will in some cases present an isolated or predominant mitral stenosis whereas other cases will show predominant incompetence

The problem of the diagnosis of the predominant mitral incompetence has received much attention in the literature during the last few years It is uni versally accepted that a loud systolic murmur at the apex is the most important sign of the presence of mitral incompetence but it is also stressed that the in competence cannot be diagnosed safely on this basis alone (*Harken et al* 1952 *Venner and Holling* 1953 *Husfeldt et al* 1953 *Soulie et al* 1953) In a few cases a predominant mitral incompetence has been operatively verified in the absence of a systolic apical murmur (*Soulie et al* 1953 *Gorlin et al* 1952 *Froment et al* 1952)

The following signs have been considered indicative of mitral incompetence Electrocardiographic and roentgenologic signs of enlargement of the left ventricle when the presence of aortic disease and hypertension can be excluded systolic expansion of the left atrium at electrokymography or fluoroscopy and a characteristic shape of the curve recording the pressure in the pulmonary capillaries traced at cardiac catheterization (*Asger Pedersen* 1955) So far none of these signs have afforded the absolutely safe guide in the diagnosis of mitral incompetence the clinical diagnosis of which is still in the crucible (*Biorck et al* 1953 *Soulie et al* 1953 *Harken et al* 1952 *Gorlin et al* 1952 *Logan and Turner* 1952 *Tybjærg Hansen* 1953 *Bridgen and Leatham* 1952)

AETIOLOGY AND PATHOGENESIS

Aetiology – It is universally agreed that in almost half the cases mitral stenosis is preceded by an acute *rheumatic infection* which is the cause of the subsequent valvular disease In the other cases the aetiology is not known with certainty This group was established as a special entity *stenose mitrale pur congenitale ou infantile* by *Duroziez* in 1877 he considered the mitral stenosis to be either congenital or acquired in childhood in patients with a special pre disposition The extensive literature on this subject has been analysed by

Temerson (1938) who concluded that the congenital origin of this type of the disease has never been proved and that it was most probably of inflammatory possibly *rheumatic* origin As this type shows essentially the same course as the definitely rheumatic cases it has now become customary to collect all cases of cicatricial mitral stenosis in the group of *rheumatic mitral stenosis*

✓ *Congenital* mitral stenosis is known but most frequently seen in infants and is then combined with other congenital anomalies of the heart such as ductus arteriosus coarctation of the aorta or interventricular septal defect (*Ferencz et al* 1954 *Abbott* 1936) Congenital mitral stenosis has also been described in adults in conjunction with interatrial septal defect (*Lutembacher* 1916 *McGinn and White* 1933 *Roessler* 1934 *Bedford et al* 1941 *Courter et al* 1948) even though it is not always in these cases easy to decide whether the mitral stenosis is rheumatic or congenital According to present day views congenital mitral stenosis as an isolated anomaly is extremely rare (*Friedlander* 1932 *Emery and Illingworth* 1951)

It may also be mentioned that in an autopsy study on 176 old patients with calcification of the left annulus fibrosus *Geill* (1952) found sclerosis and slight stenosis of the mitral valves in a few cases he pointed out however that the mitral stenosis was but slight and not the cause of death

✓ It may thus be assumed that neither the congenital nor the sclerotic mitral stenosis plays any essential part as aetiologic cause of the ordinary mitral stenosis in adults✓

✓ *Development of mitral stenosis* – [The acute rheumatic infection produces an acute mitral valvulitis with specific rheumatic infiltrates in the connective tissue apparatus of the valves and in the chordæ tendineæ At the stage of healing the chordæ and the valves shrivel and thus become considerably de formed If during the acute stage the valves agglutinate adhesions result and the valvular stenosis thus develops]

[In cases of chronic mitral stenosis the adhesion of the valves may be so extensive that only a rigid diaphragm or tube with a narrow ostium is left instead of the normal freely movable valves In addition the valves are not infrequently sclerosed and eroded]

[If the valves do not fuse the shrivelling of the valves and the chordæ tendineæ will result in a pure mitral incompetence but as previously mentioned a vary ing degree of mitral incompetence is no infrequent occurrence in mitral stenosis as the rigid non resilient valvular apparatus is incapable of closing completely during the ventricular systole

We have no safe methods by which to estimate for how long a time the rheumatic process in the valves is active However it has been ascertained in follow up studies in patients with rheumatic fever that the fully developed mitral stenosis will seldom have been established during the first few years

after the rheumatic fever and in most cases the development takes up to from 6 to 8 years (*Sheldon* 1930 *Mackie* 1926 and *Cohn* 1927)

Bland and Jones who have the greatest experience with regard to the development of valvular disease after rheumatic infection as they have observed 1000 children during 20 years after the initial infection have seen the mitral stenosis develop after a much longer period Among 347 patients who presented no signs of valvular disease after the initial infection *Bland and Jones* observed the development of definite valvular disease (in most cases mitral stenosis) in 83 patients in the course of the first ten years and in further 71 patients in the course of the next decade a considerable number of cases setting on between the fifteenth and the twentieth year after the primary infection (*Bland and Jones* 1951) Only one third of these 154 patients with valvular disease that had developed later presented definite clinical signs of rheumatic recurrences With regard to the other two thirds *Bland and Jones* themselves were in doubt how to explain the development of the valvular disease they put forward the hypothesis that repeated depositions of thrombi of blood platelets might take place in small cicatrices in the valves and in the course of time become incorporated in the valvular tissue thus leading to the final deformation and stenosis

Duration of the rheumatic activity in the heart

The patho anatomists have been inclined to consider the histological demonstration of Aschoff s nodules described by *Aschoff* in 1904 and demonstrated 2 years earlier in Copenhagen by *J Stein* (1902) as specific of rheumatic fever and its sequelae (*Boyd* 1938) Even though this view is not shared by all investigators it is of great interest that the incidence of Aschoff nodules in the heart (especially in the myocardium) is great in series of autopsied cases of rheumatic valvular disease

In autopsy investigation of 161 cases of rheumatic heart disease *Rothschild Kugel and Gross* (1934) found macroscopical or microscopical signs of active rheumatic infection in 106 patients including 95 with Aschoff nodules The incidence of rheumatic activity in relation to age in this series is shown in the table below –

Incidence of Histological Si ns of Rheumatic Activity in Rheumatic Heart D sease

Age at death	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	years
Rothsch ld et al	100	95	78	70	38	13	12	0%	positive findings
Juca and White	–	–	31	6	25	17	8	(20)	

Juca and White (1944) whose results in a series of 100 autopsied cases of rheumatic heart disease over 20 years are given in the same table found a somewhat lower incidence of histologically demonstrable rheumatic activity though both series show the same tendency to decreasing incidence of positive findings of Aschoff nodules with advancing age at death

Unfortunately it is not possible in these series of cases to compare the clinical signs of rheumatic activity with the histological findings but a point of interest is that the average time interval between the initial rheumatic infection and the occurrence of death is 20 years in *Juca and White's* series

There are numerous investigations of the past 4 years which show the incidence of Aschoff nodules in auricles removed at operations for mitral stenosis In all cases the result of preceding clinical examination was that the patients could be considered free from rheumatic activity it is therefore of great interest that characteristic Aschoff nodules are found in these – admittedly mostly small – series with a frequency varying from 17 per cent to 67 per cent being most frequently between 30 per cent and 50 per cent (*Pinniger* 1951 *Janton et al* 1952 *Sabiston and Follis* 1952 *Waaler* 1952 *Kuschner et al* 1951 *Biorck et al* 1952 *Wylie* 1952 *Enticknap* 1953 *McKeown* 1953)

The largest series of this nature has been published by *Decker et al* (1953) who found Aschoff nodules in 83 out of 183 cases (45 per cent) This series has been analysed clinically by *McNeely et al* (1953) who found that no correlation could be demonstrated between the histological findings and the clinical signs suggesting rheumatic activity (temperature leukocyte figure erythrocyte sedimentation rate increased antistreptolysin titre or electrocardiographic changes) Nor was there any correlation between the period following the rheumatic initial infection and positive findings of Aschoff nodules But the incidence of positive findings was falling with advancing age thus there were 73 per cent of positive findings in the age group 20–30 years 51 per cent in the group *30–40 years* 24 per cent in the group 40–50 years and 8 per cent in the group over 50 years Among 86 patients with sinus rhythm there were 76 per cent of positive findings and among 95 with auricular fibrillation there were positive findings in 17 per cent

We have no definite knowledge of the significance of the histological signs of rheumatic activity mentioned here but the possibility cannot be excluded that they *may* be indicative of an active rheumatic process in the heart If this is so it must be established that we possess no clinical methods by means of which it can be decided with a fair degree of accuracy whether an active rheumatic carditis is present

Thus we cannot today decide with certainty to what extent the progression of the mitral stenosis is determined by *active rheumatic processes in the valves* or in the myocardium nor can we judge to what extent the ultimate failure of the heart is the outcome of active rheumatic changes which are not clinically

recognizable or solely determined by the mechanical circulatory obstruction which mitral stenosis represents

PATHOPHYSIOLOGY

Pathophysiologically the developed mitral stenosis represents an obstruction to the inflow of blood into the left ventricle This results in an accumulation of blood and a rise in the pressure in the left atrium From here these changes spread backwards through pulmonary veins capillaries and arteries to the right ventricle

Therefore in mitral stenosis we generally find enlargement and dilatation of the left atrium and an increased amount of blood in the pulmonary circulation

As it is chiefly the right ventricle that is responsible for the compensation this will also gradually become enlarged and at last dilate When the right ventricle fails symptoms of congestive failure will appear in the venous system

This view of the pathophysiology of mitral stenosis has developed on the basis of pathologic anatomical and clinical experiences and can be found consistently described by *Steven* as early as in 1847 He also drew attention to the fact that acute accentuations in the circulatory disturbance might lead to acute pulmonary oedema

However it was not until 100 years later that this view of the pathophysiology of mitral stenosis was verified in man by means of cardiac catheterization and pressure measurements during surgical operation

The technique of cardiac catheterization was elaborated at *Cournand's* laboratory in New York *(Cournand and Ranges* 1941) That the pressure is increased in the right ventricle in mitral stenosis in man was first demonstrated with this technique at *Cournand* s laboratory in 1946 (*Bloomfield et al* 1946) The next year the increase of pressure in the pulmonary arteries in mitral stenosis was verified (*Cournand* 1947)

In 1949 *Hellems Haynes and Dexter* (*Hellems et al* 1949) and *Lagerlof and Werko* (1949) showed independently of one another that by wedging the tip of the cardiac catheter in a branch of the pulmonary artery it was possible to trace a pulmonary capillary curve which was almost identical with the pressure curve recorded in the left atrium

During recent years numerous publications have appeared showing that almost all cases of mitral stenosis which give rise to symptoms have an increased pressure at rest in pulmonary veins and arteries and in the right ventricle (*Lagerlof et al* 1949 (b) *Dexter et al* 1950 *Bayliss et al* 1950 *Borden et al* 1950 *Lenegre* 1950 *Draper et al* 1951 *Ellis et al* 1951 *Soulie et al* 1951 *Eliasch* 1952 *Lewis et al* 1952 *Janton et al* 1952 *Husfeldt and Warburg*

1951 *Baker et al* 1952 *Husfeldt et al* 1953 *Davies et al* 1953 *Epps and Adler* 1953 *Soulie et al* 1953 *Logan and Turner* 1953)

Besides affording a valuable confirmation of the classic interpretation of the pathophysiology of mitral stenosis by verifying the increase in pressure in the pulmonary circulation and in the right ventricle the technique of cardiac catheterization has given us another important clue to the comprehension of mitral stenosis

The literature today contains several numerically large series of mitral stenoses that have been operated on and which were examined with cardiac catheterization before and after mitral valvulotomy The e investigations have shown that in the cases in which the surgeon was able to perform successful mitral valvulotomy it was very often possible to ascertain a distinct fall in pressure in the pulmonary circulation in some cases the pressure even fell to normal values (*Draper et al* 1951 *Cournand et al* 1951 *Corlin et al* 1951 *Bayer et al* 1951 *Crafoord et al* 1951 *Husfeldt and Warburg* 1951 *Holling* 1952 *Husfeldt et al* 1953 *Janton et al* 1953 *Baker et al* 1953 *Soulie et al* 1953 *Logan and Turner* 1953)

Even though these studies cannot be considered concluded and even though they present many other problems which will not be dealt with here there can hardly be any doubt that they show that *the valvular stenosis per se* as a mechanical factor plays an essential role in the pulmonary hypertension in mitral stenosis

CHAPTER II

Previous Prognostic Investigations in Mitral Stenosis

In a study on retrecissement mitral pur *Duro ie* in 187 said as follows about the prognosis in the clinically pure mitral stenosis Le retrecissement mitral pur tue rarement les autopsies nous paraissent rares nous entendons de retrecissement sans dilatation meme de l oreillette Il y a un double pronostic a po er Combien peut durer un retrecissement sans accidents entravant les occupations habituelles? Combien peut il durer lorsque les complications sont etablies?

Il y aura un travail important a faire sur les complications successives qui apparaissent (*Duro ie*)

He stressed in the same work that the prognosis of the clinically isolated mitral stenosis was considerably better than had been previously assumed He enlarged on this viewpoint in 1883 complaining that in mentioning this subject previous authors had not produced any material to prove the correctness of their statements about the sinister prognosis of mitral stenosis

Duro ie himself reported the cases of 35 patients over 50 years of age with isolated or complicated mitral stenosis 9 of these patients had an isolated mitral stenosis and represented 13 per cent of his total series of cases of isolated mitral stenosis 11 patients with isolated mitral stenosis died at ages between 42 and 58 years the average age at death being 52 years for males and 58 years for females *Duro ie* further mentioned that he himself had followed several cases for more than 15 years and that several of the patients still had a good prognosis judged by their condition

In spite of the fact that *Duro ie* laid down the lines to be followed in systematic investigations into the long term prognosis of mitral stenosis at such an early date the literature contains but few large publications on this subject

In the present chapter mention will be made of the main features of the available systematic studies whereas details will be mentioned only in relation to the results of the writer s investigations reported in the following

In 1923 *Willius* in the U S A undertook a follow up examination of 470 cases of mitral stenosis and managed to trace 347 patients (82 per cent) The

period of observation was not exactly stated but was said to cover a 6 year period 153 out of the total of 317 patients died (41 per cent) including 128 who died of heart disease after a period averaging 15 [illegible] months Of the 194 survivors 30 had improved in 102 the condition was unchanged and in 62 it had aggravated

Among 90 patients with auricular fibrillation 58 (6[illegible] per cent) died during the same period including 51 who died of heart disease after a period averaging 22 8 months Of 50 patients with significantly negative T waves (T_1 T T_3 negative in all combinations) 62 5 per cent died of heart disease after a period averaging 12 1 months

Of 253 patients with isolated diastolic presystolic murmur 45 5 per cent died after a period averaging 13 [illegible] months and of 197 patients with combined systolic and diastolic or presystolic murmur a total of 29 0 per cent died after a period averaging 17 1 months

No detailed analysis of the correlations of the influence on the lethality of the individual factors mentioned was made (*Willius* 1923)

In 1935 *DeGraff and Lingg* published a large work on the course of rheumatic heart disease in adults They based their studies on a series of cases comprising 1633 patients over 15 years who had been examined during a 10 year period at heart clinics and at 2 private practices in New York They managed to trace 1253 (77 per cent) of these patients Their statement of results is based solely upon the 644 patients who died during the period of observation The surviving 609 patients were not considered by the authors as they thought that the course of the disease in this group would not essentially change the total picture since the survivors had a shorter duration of the disease than those who died

In the series of 644 patients [illegible] per cent had isolated mitral disease (mitral stenosis or mitral stenosis plus incompetence) and 28 6 per cent had mitral and aortic disease while 4 5 per cent suffered from mitral aortic tricuspid or pulmonary valve disease Almost the same average course of disease was found in the various forms of valvular disease and the average patient s course of life was given thus Rheumatic fever at the age of 17 years heart symptoms at the age of 28 heart failure at 30 and death at 33 Three fourths of all patients had died before the 43rd year and only 10 per cent survived after the 50th year

Even though the original series comprises a relatively great number of young patients it must nevertheless be doubted whether the conclusions drawn from this study are tenable partly because no details are available at all about 23 per cent of the original series – a proportion which may have included many with a long period of survival – and partly because the 609 survivors have not been considered in the analysis

In 1936 *Friedmann* published the results of a follow up of 544 cases of mitral stenosis (245 of pure mitral stenosis and 299 of mitral stenosis plus incompetence) The period of observation ranged from 1 to 16 years and the author calculated the excess lethality in relation to the mortality in the Austrian normal population He did not describe the series of cases in greater detail He found a lethality of +123 per cent in the case of pure mitral stenoses and of +179 per cent in the case of combined mitral stenosis and mitral incompetence Among males only the lethality percentages were +173 and +172 per cent respectively and among females +104 and +182 per cent for pure mitral stenosis and combined mitral stenosis plus incompetence

The excess lethality was highest in the age group 40–50 years and this special excess lethality proved to be independent of the time when the valvular disease had developed

*Aastrup*s prognostic studies on the basis of electrocardiograms include a follow up of 90 cases of mitral stenosis 50 being dead after 6 to 10 years In the following mention of the separate problems of mitral stenosis reference will often be made to this series (*Aastrup* 1937)

The most important contribution to the study of the prognosis in mitral stenosis has been afforded by *Grant* (1933) His series comprised 238 men with isolated mitral stenosis all ex servicemen from World War I and the whole series was observed during 10 years It had been collected to form part of the prognostic studies in heart disease planned by *Lewis* The diagnosis had been verified by the demonstration of a diastolic and/or presystolic apical murmur and the series was divided into 4 functional groups according to the results of functional tests The size of the heart was estimated by palpation and divided into 4 grades The original series especially comprised the age groups 20–29 years and 30 39 years the average age in the series thus being 31 6 years at the beginning of the observation The total analysis of the whole series (according to *Grant*s Table XXXIII) after 10 years shows that 100 patients (42 per cent) died 81 patients (34 per cent) presented signs of progression of the heart disease and that the condition in 57 patients (24 per cent) had remained unchanged

Grant mentioned the following as signs of a grave prognosis Congestive failure pronounced enlargement of the heart and auricular fibrillation All patients with congestive failure died in 10 years and the average survival time for this category was stated to be from 4 to 5 years Increasing enlargement of the heart meant a poorer prognosis so that the lethality after 10 years for a normal heart was found to be 8 per cent for a slightly enlarged heart 41 per cent for medium enlargement of the heart 54 per cent and for a markedly enlarged heart 83 per cent When divided into functional groups the series showed the following differences Of the group good exercise tolerance

9 per cent died in 10 years of the group fair exercise tolerance 20 per cent of poor exercise tolerance 48 per cent and of the group congestive 100 per cent

Of the cases with auricular fibrillation 68 per cent died in 10 years According to *Grant* the prognosis was especially favourable in cases with a good capacity for physical performance and absence of congestive failure enlargement of the heart and auricular fibrillation Only 10 per cent of this group died in the course of 10 years

Grant s series is the only extensive investigation into the prognosis of mitral stenosis and reference will therefore often be made to this in the following

This publication also contains a follow up examination of 195 males with combined mitral stenosis and aortic insufficiency The average age was 29 8 years

After 10 years 42 per cent were dead 33 per cent presented signs of progression of the heart disease and 25 per cent showed unchanged conditions

No definite difference could be demonstrated in the prognoses for the group with slight and for that with pronounced aortic regurgitation as the lethality after 10 years was 35 per cent and 32 per cent respectively There was no definite difference in lethality between the groups with normal hearts and slight to medium enlargement of the heart (25 – 28 – 33 per cent) but these were separated from the group with large hearts which had a considerably higher lethality (69 per cent) The groups good fair and poor exercise tolerance showed almost the same lethality (22 – 24 – 38 per cent) whereas the poorest exercise group congestive had a 100 per cent lethality in the course of 10 years

Grant pointed out that the high incidence of subacute bacterial endocarditis in this series made it difficult to establish the prognosis on the basis of the objective findings

Grant s follow up was consistently carried through and cannot be justly criticized His series affords very valuable information on the course of mitral stenosis in males in the third and fourth decades during a 10 year period However it comprises only males and the older decades are represented by few cases only

The writer did not find other large systematic investigations into the clinical course of mitral stenosis Several publications are however available which are based upon autopsy series and illustrate the course and complications of mitral stenosis as mentioned in detail on page 82

A review of the clinical follow up examinations of the course of mitral stenosis that have been published so far shows that there are only few studies on the course of the disease in females and on the course in males in the older decades

Consequently *Bland and Jones* are right in saying that systematic clinical examination of the course of rheumatic heart disease during older decades have been scarce and that studies in fatal cases rather than in the surviving may have caused our perspective to be unfavourably distorted (*Bland and Jones* 1951)

CHAPTER III

Writer's Series of Cases

The series to be dealt with here comprises 351 patients with definite or probable mitral stenosis (isolated mitral stenosis or mitral stenosis combined with aortic valvular disease)

The material is derived from two sources and comprises (1) 285 patients who were in Medical Department B the University Hospital Copenhagen during the period from January 1st 1933 to December 31st 1949 during which period the department was in charge of Professor *Erik Warburg* M D and (2) 66 patients who in the course of the same period saw *Warburg* in private consultation

The series was selected by the writer so as to include only the patients who fulfilled the criteria mentioned on p 30 for the diagnoses of isolated mitral stenosis probable mitral stenosis and mitral stenosis combined with aortic valvular disease

In Medical Department B the University Hospital I procured the series after a study of the card index of diagnoses and of all case records for patients who during the period mentioned were discharged with diagnoses belonging to the group of rheumatic diseases of the valves of the heart

The series from *Warburg*s private consultation was selected on the same lines after I had studied all case records with diagnoses belonging to the group of rheumatic diseases of the valves of the heart

In the no small number of cases in which a patient was to be found in both original series the patient has been classed according the original series in which the earliest examination was recorded

Table 1 gives a survey of the series according to chief diagnoses and original series

Representativeness of series

The patients in Medical Department B the University Hospital Copenhagen come from all Denmark (including the Faroe Islands) and consisted during the period mentioned almost exclusively of persons over 14 years of age Only a comparatively small number of patients had been admitted with early signs of heart disease the series of this department will therefore comprise a relatively great number of patients with advanced heart disease

TABLE 1

Survey of Writer's Series according to Chief Diagnoses and Original Series

Chief diagnosis	Med Dept B University Hospital		Prof Erik Warburg [illegible]		Total		
	female	male	female	male	female	male	total
Isolated mitral stenosis	152	61	42	16	194	77	271
Probable mitral stenosis	1	9	—	—	12	9	21
Combined mitral stenosis and aortic valvular disease	25	26	6	2	31	28	59
Total	189	96	48	18	237	114	351

The series of cases from *Warburg*'s consultation comprises both young and older patients However when the series is considered as a whole in the following it cannot be avoided that the numerically much greater series from Medical Department B of the University Hospital Copenhagen will characterize the whole series this will therefore contain a relatively great number of elderly patients in an advanced phase of the disease

The present series will therefore presumably comprise a greater number of elderly and of more advanced cases than is generally seen in a regional medical department in Denmark

Examination of series at first observation

In the case of the patients admitted to Medical Department B the University Hospital Copenhagen a detailed past history and objective examination including thorough clinical examination of the heart are available from the first observation performed by the assistant physicians of the department and in the great majority of cases also by the head of the department Professor *Erik Warburg* Electrocardiography was performed in all cases and in the great majority of cases roentgenograms of the heart are available in the postero anterior position in rarer cases also in the right and left anterior oblique positions and in the sagittal position kymograms are also available in some cases The blood pressure measurements were made by the interns of the department or by medical undergraduates A Wassermann test was made

in almost all patients at Statens Seruminstitut Copenhagen Phonocardiography was performed in a number of cases with the technique described in *Frosts* thesis (1944)

The patients from *Warburgs* private consultation were examined in the same manner and electrocardiogram orthodiagram and blood pressure measurement are available in all cases

The clinical examinations of the heart formed the basis of the classification of the series in the present study

The 301 patients were traced in the course of the years 1951 to 1953 Sixty patients died during their first or subsequent stays in the department and their fates were thus settled It was attempted to trace the remaining number of patients by enquiring first at the Public Registration Offices In this manner sufficient information was obtained in 98 per cent of the cases In the rest of the cases the necessary information was obtained through the assistance of the general practitioners the health insurance societies or the families of the patients In the case of one patient information could only be obtained for a period of four years after her discharge as she had then emigrated to Germany and further search was futile Information was obtained about the fates of all the other patients in the series In the case of those who died during the period of observation further particulars were received about the date and place of death and the residence of every one surviving patient became known in the course of the follow up

The mentioned patient who could not be traced owing to emigration represents 0 3 per cent of the series and must therefore be considered of no importance to the general picture Consequently she has been left out of consideration

The percentage of patients traced was thus 99 7 for the total series and for those resident in Denmark 100 per cent

Of the 291 patients traced 94 were alive at the time of the follow up and 197 had died during the period of observation

The continued follow up was carried through in such a manner that information was first collected about the dead patients after which the surviving were followed up

Inquiry about the dead patients

This part of the series comprises 197 patients After information had been obtained about date and place of deaths the death certificates were gone over at the Public Record Office or at the Board of Health and diagnoses and causes of death were taken down In all cases a detailed questionnaire was then sent to the doctor who had issued the certificate and this was answered in detail in most of the cases

Questions were asked in all ca es about the course of the disease the most important complications possible admissions to hospital and causes of death In the case of the doctor s death the patient s relatives supplied some useful information

In cases in which it was known that the patients died in other hospitals the case records were borrowed from the departments concerned case records from other admissions to hospital during the period of observation and also of the time before the first observation have also been studied

In the case of autopsied patients the autopsy records were gone over

Inquiry about surviving patients

This part of the series comprises 94 patients The follow up of the surviving patients was undertaken for the purpose of making the greatest possible number of patients appear for control examination at Medical Department B of the University Hospital in Copenhagen An explanation of the purpose of the examination was sent as the case might require either to the general practitioner or directly to the patient and in this manner it was managed to persuade 84 out of the 94 surviving patients to appear for examination in the department However it was often necessary to write repeatedly and in no small number of cases the patients had to be called on at home to be persuaded to appear 40 of these patients were admitted for control and 44 were followed up as outpatients Only 10 patients could not be persuaded to appear for examination at the hospital Six of these were examined in their homes Four patients were not followed up and the causes hereof may be mentioned One patient was resident in Stockholm and could not spare the time to go to this country The second patient was a psychopath and a tramp and was not willing to cooperate at the follow up The third patient refused to be examined owing to illness at home The fourth patient was the only one who directly declined cooperation stating as his reason that the first examination had been too expensive and that he had not got the pills for his heart which he ought to have had

The follow up examination was a reproduction of the first examination comprising the ordinary clinical examination electrocardiography phonocardiography blood pressure measurement and roentgenograms of the heart in the postero anterior position right and left anterior oblique positions and the sagittal position with contrast medium in the oesophagus

Cardiac catheterization was performed in only few cases when surgical operation for the mitral stenosis was being considered Five of the patients followed up were subjected to mitral valvulotomy after the control examination

As in the case of other follow up examinations undertaken in this country it was endeavoured to make it as personal as possible giving the patients to understand that they too were to benefit by the results of the examination

Consequently the findings were reported to the general practitioner in as many cases as possible It was gratifying to experience the interest and confidence of the patients when they appeared for the examination

The experiences in the follow up of the present series of cases thus fully confirmed the results obtained in similar examinations in this country by *Aastrup* (1937) *Bechgaard* (1946) *Bang* (1947) and *Trolle* (1951) they all found that almost all patients can be traced and that almost all surviving patients can be persuaded to cooperate at the follow up

DIAGNOSTIC CRITERIA

In establishing the diagnostic criteria for the present series of cases the lines were followed which applied during the period in which the same cases were first examined These criteria are based upon the tradition which has been created in this country by *Warburg* s publications (1932 1943) A detailed description and discussion of these diagnostic criteria was given in *Aastrup* s large investigation into the prognostic importance of the electrocardiograms His publication was based upon a series of cases electrocardiographed by *Warburg* (*Aastrup* 1937)

In the present work isolated mitral stenosis and combined mitral stenosis and aortic valvular disease have been studied separately Mention is first made of the isolated mitral stenosis

Isolated mitral stenosis

By isolated mitral stenosis is understood the presence of a mitral valvular disease with pure or predominant stenosis without simultaneous signs of aortic valvular disease

In the present study the group isolated mitral stenosis only includes cases which either fulfil the demands of a safe clinical diagnosis or have had the mitral stenosis verified at autopsy

The clinical diagnosis of isolated mitral stenosis was based upon the presence of a rough rolling or rasping mesodiastolic or presystolic apical murmur either one or the other or both murmurs simultaneously In doubtful cases the patients were also auscultated after exercise and lying on the left side according to the statements by *Lewis* *Warburg* and others

In the presence of the characteristic apical murmur or murmurs the following findings also supported the diagnosis of isolated mitral stenosis A diastolic thrill at the apex accentuated 1st sound at the apex mitral snap accentuated 2nd pulmonary sound roentgenologically enlarged left atrium and distended pulmonary artery with straight left contour of the heart or bulging second left

arch and the electrocardiographic findings right axis deviation large P waves or auricular fibrillation or flutter

However the clinical diagnosis of mitral stenosis was established only when one or both of the characteristic murmurs were heard – and heard with certainty

When a characteristic diastolic or presystolic apical murmur was heard it was not considered in the classification of the series whether a systolic apical murmur had been heard simultaneously as the lines were followed which applied in this country during the period of the first examination of the series And when the series of cases was gone over later it was not considered possible to evaluate in which cases there might be a predominant component of incompetence (An estimate of the incidence of an appreciable component of incompetence in the series of isolated mitral stenoses is given on page 50)

As the diagnosis isolated mitral stenosis is thus based upon the findings at clinical examination of the heart it may be pointed out that the great majority of the auscultatory examinations were performed by the same examiner Professor *Erik Warburg* who took a special interest in rheumatic valvular disease during the whole period To this may be added that from 1936 phonocardiography has been used to a considerable extent in Medical Department B the University Hospital Copenhagen as a method to control the auscultatory findings This has undoubtedly contributed to the assurance of the physicians of the department in localizing the murmurs in the heart cycle Phonocardiograms are available for 57 patients of the series of isolated mitral stenoses in Department B these have verified the diastolic or presystolic murmurs that have been heard Furthermore at the follow up the writer verified the auscultatory findings of characteristic diastolic or presystolic murmurs in 50 patients See top figure page 74

Combined mitral stenosis and aortic valvular disease

This group only comprises the patients who fulfil the demands of the clinical diagnosis of combined mitral stenosis and aortic valvular disease or in whom this diagnosis was verified at autopsy

The clinical diagnosis of combined mitral stenosis and aortic valvular disease was based upon unmistakable signs of both forms of valvular disease The criteria for the clinical diagnosis of mitral stenosis have been given above and the clinical criteria for the diagnosis of aortic valvular disease were signs either of aortic incompetence or of aortic stenosis or both simultaneously

Clinical criteria of aortic incompetence – The diagnosis was established on the presence of a high pitched diastolic blowing murmur over the aorta or down along the left sternal border often with a maximum in the left third intercostal space The diagnosis was supported by the peripheral signs of aortic incompetence A swift abrupt radial pulse capillary pulsation on the forehead

arterial pulsation in the fingers pistol shot sounds in the great vessels and a high blood pressure amplitude with a low diastolic blood pressure also pronounced enlargement of the left ventricle

Clinical criteria of aortic stenosis – The diagnosis was based upon the presence of a loud harsh systolic murmur with its maximum over the aorta often transmitted into the cervical vessels and associated with at least two of the following characteristic signs faint or absent 2nd aortic sound or short diastolic murmur over the aorta a thrill over the aorta or a slow pulse When enlargement of the left ventricle could be demonstrated this supported the diagnosis

In many cases the mentioned clinical criteria for the diagnoses of the aortic valvular diseases have been combined so that it proved to be appropriate to consider the group combined mitral stenosis and aortic valvular disease as a whole in the following description

Cases in which the mentioned criteria for complicating aortic disease were not fulfilled have been included in the group of isolated mitral stenosis

With regard to the *right sided valvular diseases* it has not been endeavoured to distinguish these as special groups as the diagnosis of these is very doubtful as pointed out by *Warburg* (1932) and *Aastrup* (1937) The incidence of right sided valvular diseases will be mentioned in greater detail in dealing with the autopsy findings in the series

In classifying the series according to the criteria mentioned 271 patients of the original series could be classed as cases of isolated mitral stenosis and 59 patients could be grouped as cases of combined mitral stenosis and aortic valvular disease In further 21 patients the clinical picture was highly suggestive of mitral stenosis though the characteristic diastolic or presystolic murmur could not be heard This part of the series will be mentioned separately on page 179 under the term probable mitral stenosis

SAFETY OF THE CLINICAL DIAGNOSES

It has been attempted to verify the clinical diagnoses used in the present series of cases either by the findings at autopsy or by clinical follow up examination of the surviving patients

Safety of the clinical diagnosis of isolated mitral stenosis

The clinical diagnosis of isolated mitral stenosis based upon the finding of a characteristic diastolic and/or presystolic apical murmur without simultaneous signs of aortic valvular disease could be verified by autopsy findings in 78 cases and mitral stenosis was found in all cases It may be pointed out here that it was not *considered possible either clinically or pathologic anatomically*

to distinguish between mitral stenosis and stenosis plus mitral incompetence thus only the presence of a stenosis was considered

In 32 out of the 78 cases (41 per cent) there was sinus rhythm when the murmur affording the diagno is was heard whereas auricular fibrillation was present at the first examination in 46 cases (59 per cent)

Seventy five out of the 78 patients with clinically isolated mitral stenosis presented an isolated mitral disease at autopsy whereas 3 patients in addition to the mitral stenosis presented an aortic valvular disease which had not been previously diagnosed

The clinical diagnosis of isolated mitral stenosis could be verified at the follow up in 78 cases and the pre ence of the characteristic apical murmur was ascertained in all cases At subsequent mitral valvulotomy the presence of the mitral stenosis was verified in 5 of these patients

In this group 34 out of 78 patients (44 per cent) had sinus rhythm at the first examination whereas 44 patients (56 per cent) had auricular fibrillation when the murmur was first heard

Sixty six out of the 78 patients who presented the picture of an isolated mitral stenosis at the first examination also had an isolated mitral stenosis at the follow up while 12 patients in addition to definite signs of mitral stenosis showed unquestionable clinical signs suggesting the presence of aortic valvular disease

In all cases in which control was possible the clinical diagnosis of isolated mitral stenosis has thus proved to be a tenable and very safe diagnosis with regard to the presence of the mitral stenosis These results are in accord with *Aastrup* s experiences he found that the apical murmur in 21 patients under 20 years who suffered from mitral stenosis had not disappeared at subsequent examinations he also had the clinical diagnosis of mitral stenosis confirmed at autopsy in 21 cases (*Aastrup* 1937) The writer s results also correspond entirely to those reported in *Grant* s series of cases in which the clinical diag nosis was controlled at autopsy in 28 cases and verified in all

Aortic valvular disease which had not been diagnosed at the first examina tion was ascertained later in 3 out of 78 autopsied cases and in 12 out of 78 surviving patients followed up This finding thus represents about 4 per cent of the autopsied cases and about 15 per cent of the surviving patients followed up Even when it is assumed that the aortic valvular disease may have been established at the first examination the percentage of error is not alarmingly high However the possibility can hardly be ignored that the aortic valvular disease may have developed in a number of cases during the period of observa tion so that the actual percentage of overlooked aortic disease may possibly be somewhat lower

The question then arises How often could the characteristic murmur be heard in the cases of isolated mitral stenosis verified at autopsy?

In the total series of 85 cases of isolated mitral stenosis verified at autopsy the characteristic murmur could be heard at the apex in 75 (88 per cent.) whereas the murmur affording the diagnosis had not been heard with certainty in 10 of the patients who died

Four out of these 10 patients had not been through the systematic examination in the department before they died When these four cases are left out of consideration the characteristic murmur was heard in 75 out of 81 cases or in 93 per cent The 6 patients in whom the murmur had not been heard all had right sided heart failure were all over 40 years of age 3 over 50 and 4 had auricular fibrillation

It has thus been shown by the present series that it has been possible with some experience to establish the clinical diagnosis of mitral stenosis in 93 per cent of cases verified at autopsy and that those in which the clinical diagnosis failed were advanced cases with heart failure and in several auricular fibrillation

The safety of the clinical diagnosis of isolated mitral stenosis as compared to the findings at autopsy in the present series is thus in fine conformity with *Iastrup*'s findings of the clinical diagnosis in 21 out of 22 cases (95 per cent) with *DeGraff and Lingg*'s 95 per cent and with *Kiss*'s 90 per cent of clinical diagnoses in the autopsy series

Safety of the clinical diagnosis of combined mitral stenosis and aortic valvular disease

In the present series the safety of the clinical diagnosis of combined mitral stenosis and aortic valvular disease could be controlled at autopsy in 14 cases In 11 of these cases both diagnoses of valvular disease were correct (80 per cent) while only one or the other type of valvular disease was found at autopsy in 3 cases Two out of these 3 patients had aortic valvular disease only and 1 patient had mitral stenosis only

Thus in 11 out of 14 or in 80 per cent of the cases with the clinical diagnosis of combined mitral stenosis and aortic valvular disease the auscultatory criteria for the clinical diagnosis were corroborated

Two out of the 3 cases with a wrong diagnosis only had a combined aortic stenosis and incompetence whereas the mitral valves were found to be normal in spite of the fact that a rolling diastolic murmur had been heard at the apex This has presumably been an aortic incompetence murmur an Austin Flint murmur transmitted to the apex

In the last case that had been wrongly diagnosed only a mitral stenosis was found whereas the aortic valves were normal even though a faint systolic and a prolonged diastolic murmur had been heard at the left sternal border The pulmonary valves had not been described and there was only a slight dilata

tion of the pulmonary artery in the roentgenogram The question whether this murmur may have been one of functional pulmonary incompetence a so called Graham Steell murmur or whether it may have been caused by an organic *pulmonary incompetence cannot be definitely settled*

The safety of the clinical diagnosis of combined mitral stenosis and aortic valvular disease could be controlled at the follow up in 12 cases and the diagnosis was verified in all cases

It can thus be ascertained that the clinical diagnosis of combined mitral stenosis and aortic disease as this could be established at the first examination in the present series was verified in 11 out of 14 cases controlled at autopsy and in 12 out of 12 cases followed up When the clinical diagnosis of combined mitral stenosis and aortic disease has been established it has been so with a fair degree of safety

The next question is how often the murmurs that are decisive to the clinical diagnosis could be heard in the cases of combined mitral stenosis and aortic valvular disease which were autopsied later In the total series mitral stenosis *associated with aortic valvular disease was found at autopsy in 21* cases in all No distinction is made here between aortic stenosis and incompetence either pathologic anatomically or clinically Two out of these 21 patients died very soon after admission before a systematic examination could be undertaken and thus without the valvular diseases having been clinically diagnosed These 2 cases are therefore not considered in the following discussion

Both types of valvular disease had been correctly diagnosed in 11 out of the remaining 19 cases (58 per cent) of mitral aortic disease verified at autopsy In 5 the aortic disease had been correctly diagnosed whereas the mitral stenosis had not been heard In 3 patients the mitral stenosis had been correctly diag nosed while the aortic disease had been overlooked in 2 and supposed in 1 Both types of valvular disease had thus been correctly diagnosed in 11 out of 19 patients or in about three fifths of the cases of combined mitral stenosis and aortic valvular disease verified at autopsy The mitral stenosis had been correctly diagnosed in 14 out of 19 patients or in three fourths of the cases whereas this diagnosis had failed in one fourth Finally the aortic valvular disease had been correctly diagnosed in 16 out of 19 patients or in about five sixths of the cases this diagnosis thus failed in only one sixth

There will thus be rather a considerable uncertainty in the clinical diagnosis of the combined mitral stenosis and aortic valvular disease a fact that is well known in the literature and has been discussed by *Aastrup* among others This series shows a fairly good conformity with *Aastrup*s experiences and the writer s results closely correspond to the findings in *DeGraff and Lingg* s series in which the clinical diagnosis had been established in 60 per cent of the autopsied cases In *Kiss* s series the clinical diagnosis was correct in 62 per cent

Thus the clinical diagnosis of combined mitral stenosis and aortic valvular

disease compared with the diagnosis established at autopsy has been found to be less safe than that of the isolated mitral stenosis

When these findings are compared with the above mentioned experience that subsequent examinations have shown the presence of mitral stenosis associated with aortic valvular disease in patients who only presented an isolated mitral stenosis at the first examination it must be admitted that we are unable to draw quite definite limits between these two groups

ROENTGENOLOGIC CRITERIA

Roentgenologic examination of heart and lungs was undertaken to the greatest possible extent in the present series of cases being omitted in only few patients who had been admitted in a very exhausted condition

In the case of the outpatients the roentgenologic examination was performed as orthodiagraphy by *Warburg* In the other patients the examination was performed as ordinary roentgenography with a film focus distance of 2 metres In most of these cases an exposure in the postero anterior position only is available In one third of the cases there is also an exposure in the right anterior oblique position as a rule with contrast medium in the oesophagus Exposures in the left anterior oblique position and in the lateral position are available only in less than 10 per cent of the cases and these exposures will therefore not be considered in the following

In studying the roentgenologic material I kept three things in view First to assess the total size of the heart secondly to attempt an estimate of the changes in the shape of the heart and thirdly to evaluate the amount of blood in the pulmonary circulation

Size of the heart

Numerous methods have been described by which to estimate the size of the heart at roentgenologic examination these may be single methods based upon measurement of single diameters which are judged in relation to individual factors such as width of the chest circumference of the chest height weight or other factors But there are also more complicated methods such as *measurement of the frontal area of the heart or three dimensional determina*tion of the volume However no matter which method is used it appears that the limit between the normal and the definitely enlarged heart is doubtful and varying

For practical reasons which will be mentioned later I chose in the present series to use *Groedel*s heart lung quotient as a measure of the size of the heart this is the ratio between the greatest transverse shadow of the heart and the

inner diameter of the thorax immediately above the cupola of the diaphragm (*Groedel* 1918) I preferred to express the ratio as the *cardio thoracic index* which states how many per cent the transverse diameter of the heart is of the inner lower width of the thorax The transverse diameter of the heart was measured as the sum of the distances from the midline to the extreme points on the right and left borders of the heart and the width of the thorax was measured as the inner distance between the costal margins at the level of the vault of the diaphragm

The roentgenograms were taken in a medium position of expiration and it appears from the table below showing the variations in the cardio thoracic index at repeated examinations in the same patient at short intervals that the cardio thoracic index found could be reproduced with great certainty with the technique employed

TABLE 2

Variations in the Cardio thoracic Indices at Repeated Examinations

45–45	52–53	56–59	65–66
45–44	5[illegible]–53–55	56–[illegible]8–57	64–66
47–50	53 54	57–58	64–65
48–48	53–54	57–59	67–66–67
48–49	53 55	58–[illegible]7	67–67
48–48–49	53–56–54–5	58–58	68–68
49–48–46	55–55	59–56–55	68–71
50–49	55–55	59–59	69–69–71
50–51	55 56	59–59	69–69
51–52	55 59	60–60	70–71–71–69
[illegible]1–51–[illegible]1–51–5	56–55	60–62–61–61	7[illegible]–71–71
52–50	56–54	62–62	[illegible]4–76
5[illegible]–50	56 57	62–63	80–81
52–52–53			

The indices given above were calculated by the writer on the basis of his own measurements on the roentgen films each figure being the mean of three measurements read in millimetres

In the case of the orthodiagrams the measurements performed by *Warburg* were used

As already mentioned the greater part of the roentgenologic material was available in the form of teleroentgenograms taken at a distance of 2 metres a smaller part being orthodiagrams When the cardio thoracic index is to be compared in the two materials it is necessary to consider that the measures of the transverse shadow of the heart and the width of the thorax differ with the two methods The orthodiagrams give the correct figures as the rays are parallel with this method of examination In the case of teleroentgenography

the transverse shadow of the heart is enlarged owing to the slightly divergent rays but at the same time the width of the thorax becomes somewhat greater in per cent so that according to *Warburg* (1913) the cardio thoracic index becomes over 5 per cent too low As most of the material was in the form of roentgenograms at a distance of 2 metres it was decided for practical reasons to use the cardio thoracic index found at roentgenography as standard consequently the orthodiagraphic cardio thoracic indices were reduced by 5 per cent in order that the material might be considered as a whole

TABLE 3

Comparison between Orthodiagrams and Roentgenograms in 7 Patients Examined in both Ways at one Day s Interval

Transverse shadow of the heart		Width of the thorax		Cardio thoracic index	
Orthodiagram	Roentgenogram	Orthodiagram	Roentgenogram	Orthodiagram	Roentgenogram
12 [illegible]	12	23 5	25 5	53	49
14 0	15 0	[illegible]6 0	29 1	54	51
[illegible]	16 3	24 [illegible]	26 9	64	61
[illegible]	16 5	[illegible]3 5	26 4	66	6[illegible]
[illegible]	[illegible]	[illegible]3 0	[illegible]4 5	69	[illegible]
[illegible]	[illegible]	[illegible]9 0	31	56	[illegible]4
16 4	17 [illegible]	23 0	26 0	71	66
[illegible]	16 0	[illegible]4 6	27 1	62	59
		Average values			

That this method is justifiable appears from Table 3 which gives comparisons between the transverse shadow of the heart the width of the thorax and the cardio thoracic index determined at orthodiagraphy and roentgenography at one day s interval in 7 patients In 6 out of the 7 patients the cardio thoracic index is lower at roentgenography and the average fall in the whole group is from an index of 62 at orthodiagraphy to one of 59 at roentgenography i e a fall of 5 per cent

Normal and pathological cardio thoracic index

As has been thoroughly discussed by *Bang* (1947) it is very difficult to draw the limit between normal and pathological values of the cardio thoracic index In the literature the following upper limits are given for the normal cardio thoracic index determined at orthodiagraphy *Groedel* (1918) 53 per cent

Hol mann (1939) 55 per cent *White* (1943) 57 per cent and *Hammer* (1918) 59 per cent *Bang* fixes a limit which however is said not to be definite at 54 per cent determined at roentgenography at a distance of 3 metres

It may be mentioned in this connection that the use of the cardio thoracic index as a measure of the size of the heart has been criticized by several authors they have stated that the cardio thoracic index varies with the width of the thorax so that normally the index will be falling with increasing width of the thorax (*Ludwig* 1939 *Comeau and White* 1942) This must undoubtedly be of importance when the limit between normal and pathological cardio thoracic indices is to be determined in the two sexes as women have a lower average width of the thorax than men Consequently it must be expected that the limit has to be fixed at a somewhat lower value for men than for women

In the present work no definite limit has been fixed between the normal and the pathological index Instead the indices of the whole series are given in the following and where it has been necessary the cardio thoracic index has been divided for the purpose of comparison into 4 groups (1) index below 51 (2) index from 51 to 54 (3) index from 55 to 64 and (4) index over 64

After a preliminary study of the series this classification was chosen because it was attempted to assess in the case of the low indices whether the upper limit of the normal was nearest 50 or 55 and whether there was any difference between men and women within this range The group with a cardio thoracic index of over 64 was considered separately in order to see whether the very large hearts had an especially bad prognosis

The possibility of using a measure of the size of the heart other than the cardio thoracic index was of course also considered It may be mentioned that it was attempted to use the transverse diameter of the heart in relation to a height weight standard as a measure of the size of the heart (*Hodges Eyster* s formula modified by *Kurt* as given in *White* s textbook) However this method had no advantages over the cardio thoracic index that had been used either in the clinical analysis or at the estimate of the prognosis As the method could only be used in part of the series because data about weight and height were not available in a number of the ambulant patients further use of this measure was abandoned The three dimension determination of volume could not be carried through as there were no exposures in the lateral position in most of the cases

Significance of a high cardio thoracic index

When the cardio thoracic index shows a high value this will of course be due to the fact that the transverse diameter of the heart is increased The transverse diameter of the heart generally covers the shadows of the right atrium the right ventricle and the left ventricle in the postero anterior position and an increased transverse diameter may be due to dilatation of one or more

of these chambers In the case of considerable dilatation of the left atrium there may also be an increase of the transverse diameter As the cardio thoracic index only considers the dilatation of the heart in the postero anterior position it is evident that it must in itself be rather a rough expression of the changes in the heart

The determination of the cardio thoracic index will be of greater value if it can be combined with a statement of which parts of the heart have dilated In the present series however the size of the separate chambers could only be estimated to rather a limited extent as an exposure in the postero anterior position only was available in most cases

Assessment of the changes in the shape of the heart

The changes in the shape of the heart to which special importance was attached in the present work were the roentgenologic signs of dilatation of the left atrium and of the right ventricle characteristic of mitral stenosis Furthermore the signs of dilatation of the left ventricle which are of special interest in cases with complicating aortic disease were considered In establishing the roentgenologic criteria the fact also had to be considered that conditions could be estimated only in the postero anterior position in the great majority of cases

The left atrium – When this is enlarged in the case of mitral stenosis it is generally seen at the earliest in exposures in the right anterior oblique position or in lateral exposures with contrast medium in the oesophagus as the left atrium then forms an impression into the shadow of the contrast medium The left atrium then enlarges to the right and can then often be seen in hard pictures shining through the shadow of the right atrium to the right of the sternum in the exposure in the postero anterior position At the same time there may appear a dilatation of the left auricular appendix which can be seen to bulge on the left contour of the heart below the pulmonary artery In the case of continued dilatation the left atrium may form a ridge on the right side and in pronounced cases form the whole right contour of the heart In some cases there may also be a pronounced bulging of the left atrium on the left contour of the heart It happens not infrequently that the left atrium dilates upwards *it may then dislocate the left main bronchus proximally and possibly also compress* it as the atrium widens the angle between the two main bronchi

Enlargement of the right ventricle – When the right ventricle is enlarged the exposure in the postero anterior position shows that the heart has increased in width without being elongated at the same time and without increase in size of the lower left arch At the same time the conus arteriosus becomes elongated so that the pulmonary artery is seen to bulge more than usual on the left contour of the heart in the exposure in the postero anterior position The simul

taneous dilatation of the left atrium will also cause an upward and outward displacement of the pulmonary artery Owing to these two facts the left second arch of the heart will protrude more than usual so that the normal waist of the heart will be effaced and be replaced by a straight left contour or by a distinct bulging of the pulmonary artery and possibly also of the left atrium

Enlargement of the left ventricle – In the case of enlargement of the left ventricle it is seen in the exposure in the postero anterior position that the lower left arch of the heart becomes larger and longer In the cases where this finding was pronounced the left ventricle was considered enlarged It may however be mentioned that the same change of contour may undoubtedly though seldom be produced in the case of isolated dilatation of the right ventricle as this will then displace the left ventricle anteriorly

In estimating exposures in the postero anterior position only it was attempted to elucidate the following three points Whether there was an enlargement of the left atrium whether the left border of the heart was straight or whether there was bulging of the second left arch and whether there were signs of enlargement of the left ventricle

By additional exposures in the right anterior oblique position it was possible to assess the early and slight dilatations of the left atrium The procedure was followed to term the left atrium slightly enlarged when it was visible only in the oblique position moderately enlarged when visualized in the postero anterior position without forming the whole of the right contour and much enlarged when it formed the whole of the right contour of the heart

In cases with exposures in the left anterior oblique position the left ventricle was termed enlarged when the shadow of the heart covered in its width over 25 per cent of the spine provided that it was considered that the roentgenogram had been taken with the patient in a position of rotation of 45 degrees in accordance with *Eek* s statements (1949) It must be stressed again here that this procedure is not always correct as a dilatation of the right ventricle may undoubtedly present the same picture in some cases (*Eek* 1949 *Schwedel* 1947)

Assessment of vascular changes of the lungs – This was attempted in the form of a mere estimate care being taken to distinguish between normal doubtfully increased and definitely increased hilar markings separately and vascular markings of the lungs separately

ELECTROCARDIOGRAPHIC CRITERIA

A set of electrocardiograms in the three standard leads (limb leads) is available in almost all cases of the series

The QRS axis was estimated by means of a table given by *Wilson and Hermann* (1920) according to which the QRS axis was read in 30 degree intervals

The principle is that a knowledge of the sign and of the relative size of the waves in the QRS complex in the three standard leads is sufficient to determine the mean axis of the QRS complex within 30 degree intervals The method has been previously described and used by *Cotsche and Warburg* (1951) The diagram used is shown in Fig 1 where e_1 e and e_3 give the area between the waves of the QRS complex and the iso electric line in the first second and third standard leads the areas being positive or negative according to their position *above* or *below* the iso electric line

The P waves were considered increased in width when they measured more than 0 13 second and increased in height when they measured more than 2 0 mm in the case of P_1 2 5 mm in the case of P and 1 8 mm in the case of P_3 the criteria given by *Warburg* (1943 pp 111–112) being used (One mm –

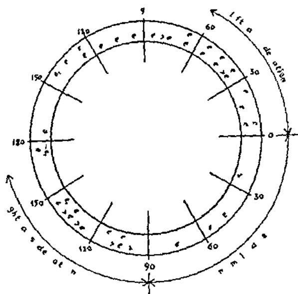


Fig 1
Diagram used in determination of the electric axis
For explanation see text

0 1 mV) Abnormal splitting of the P waves has only been considered when the splitting extended as far as to the iso electric line

The PQ interval was termed prolonged when it measured over 0 22 second (*Warburg*)

The QRS complex was considered increased in width when it measured more than 0 12 second (*Warburg*)

The T waves were termed positive when they measured more than +1 0 mm iso electric when they measured between +1 0 and —1 0 mm and negative when they measured under —1 0 mm

CLINICAL CRITERIA

The clinical criteria used were those generally accepted in the literature and only a few will be commented on

Right heart failure – This was considered only in the presence of an objectively demonstrated right sided heart failure with such signs as enlargement of the liver ascites oedemas venous congestion on the neck or a measured venous pressure exceeding 120 mm water Oedemas only were not considered indicative of right sided heart failure and enlargement of the liver was present in practically all cases

Cardiac asthma – acute pulmonary oedema – These were accepted only when there was a detailed description of dyspnoea setting on by attacks with wheezing in the chest cough frothy expectoration containing blood in some cases of a duration of at least 15–30 minutes (cardiac asthma) and preferably exceeding from 1 to 2 hours (acute pulmonary oedema)

Pulmonary embolism with pulmonary infarction – This condition has been clinically diagnosed in the presence of dyspnoea setting on acutely with cough stitch blood tinged expectoration fever and signs of pleurisy or pulmonary infiltration or in rarer cases when the patient presented the picture of acute dyspnoea followed by prolonged fever and signs of pleurisy or pulmonary infiltration not responding to treatment with antibiotics

Haemoptyses – Bloody expectoration was seen both in the group with acute pulmonary oedema and in the cases with pulmonary infarction but apart from these a few cases of haemoptysis were observed which could not be classified in the two mentioned groups and were therefore grouped among haemoptyses

Arterial emboli in the systemic circulation – These were diagnosed from the usual clinical criteria

Auricular fibrillation – This was only considered when the symptom had been verified electrocardiographically or in a few cases when it had been verified by a specialist in internal medicine Auricular fibrillation and flutter are considered together under the term *auricular fibrillation*

Functional capacity – On the basis of the available information about the cardiac complaints of the patients and the statements of their capacity for work it was attempted to divide the series into the four classes established by the *American Heart Association* for the assessment of the heart failure (1939)

The classification is as follows –

Class I – Without limitation of physical activity Ordinary physical activity causes no discomfort

Class II – Slight to moderate limitation of physical activity Ordinary physical activity causes discomfort

Class III – Moderate to great limitation of physical activity Less than ordinary physical activity causes discomfort

Class IV – Unable to carry on any physical activity without discomfort

The present series contained no cases which could be grouped with certainty in Class I With regard to the grouping in Classes II–IV it may be mentioned that Class IV generally was easily distinguished Classes II and III correspond to slight and markedly relative heart failure and except for the difficulties that may be caused in classification by intercurrent infections or other transitory disorders it appears from the definition of the two classes that the distinction between them is not sharp but subject to the personal estimate of the examiner

The writer used the following principles –

Patients who were able to walk almost without limitation on a level road but were troubled when they walked uphill or upstairs at ordinary pace and had hitherto managed their work though with slight discomfort were grouped *with Class II*

Patients who could walk only a few hundred metres on a level road who felt pronounced discomfort uphill or upstairs and who felt considerable discomfort when they went shopping or did ordinary domestic work (females) or had had to find light physical work or had had to abandon this (males) were grouped with Class III

With this classification all patients with orthopnoea and almost all with attacks of dyspnoea have been grouped with Class III or IV

PRINCIPLES IN ASSESSMENT OF THE PROGNOSIS

In forming an estimate of the prognosis i e the survival or the lethality in a group of patients after a limited period of observation it is first and fore most of importance that sufficient information is available about all patients in the original series at the end of the examination As previously mentioned the recovery percentage was 100 in the present series

Next it is a very important point that both the patients that *died* during the period of observation and those who were *alive* at the time of the follow up examination are considered in analysing the prognosis

One of the most frequent mistakes in the medical literature on prognoses is the statement of survival times which is based only on the data relating to the observed *dead* patients It has generally been argued that it was intended to state the average survival time from the date chosen Only the cases in which the patients died afforded safe information about the survival time and as it was only desired to state what was known with certainty particulars could be given only about those who died during the period of observation It is however of the utmost importance that it should be realized that information is then given only about a special group in a series and not about the whole series And it must be stressed that the special group then dealt with is not representative of the whole series with regard to the survival time The group of dead patients will comprise all cases in which the course of the disease was shortest and those in which it was longest will be included in the group of surviving patients Furthermore it is evident that the arithmetical mean duration of life calculated from the group of dead patients will be highly dependent on the length of the period of observation and will increase with this

When it is intended to find an expression of the survival of the whole group of patients both the *dead* and the *surviving* patients must therefore be considered

TECHNIQUE EMPLOYED IN ASSESSING THE PROGNOSIS

The purpose of the prognosis investigations was to express numerically how long the patients with mitral stenosis survived after the first examination or after important events in the course of the disease

As the lethality during the period of observation was found to be exceedingly high it proved to be inexpedient to express the lethality in the present series of cases in relation to the mortality in the Danish population for instance in the form of the excess mortality percentage It was decided instead to give the survival curve found for the whole period of examination As the series

has a period of observation varying from 3 to 20 years the *indirect* or actuarial method of calculating the survival was used in order to utilize the experiences as much as possible this method has been described especially in the medical literature by *Berkson and co workers* (*Berkson et al* 1950 *Burchell et al* 1951).

The principle of the method is that by calculating the annual probability of death the survival percentage is found for every year The survival curve is drawn on the basis of the annual survival percentages The method is demonstrated in the example given below

TABLE 4
Example of Survival Calculation
(Total Series of Mitral Stenoses in Women)

1	2	3	4	5	6	
I t rv l fter 1 t m f Y	St		T t l mbe f rv g t t g g f y	P y p d t de	P b b l ty f d th q	S rv l p c t g l
	D th	S g				
0–1	31	–	19	19	0.161	100
1–2	15	1	161	160.5	0.093	83.2
2–3	13	1	145	144.5	0.090	76.1
3–4	8	7	131	127.5	0.063	69.3
4–5	4	10	116	111	0.036	64.9
5–6	10	4	102	100	0.100	62.6
6–7	9	4	88	86	0.105	56.3
7–8	6	3	75	73.5	0.082	50.4
8–9	5	2	66	65	0.077	46.3
9–10	4	9	59	54.5	0.073	42.7
10–11	2	1	46	45.5	0.044	39.6
11–12	6	–	43	43	0.140	37.9
12–13	–	2	37	36	–	32.6
13+	11	24	35	–	–	32.6

Column 1 in the table above gives the interval between the first examination and the follow up examination Column 2 shows the number of deaths for any one interval so that all who died within 1 year after the first examination are placed in the group at the interval 0–1 year all who died between the first and second years are placed at this interval and so on Similarly column 3 is filled in for surviving cases for each interval

Column 4 gives the number of persons who were alive at the beginning of this interval The figure is most easily calculated by cumulative addition of columns 2 and 3 from below At the interval 13+ the figures 11 and 24 are added The sum 35 is entered in column 4 at the bottom For the year above

35 is then added to 2 in column 3 and to 0 in column 2 + 3. For the year above this figure we have 37 + 6 = 43 and so on. The rest of the columns are filled in by calculation on the basis of the figures in columns 2 to 4. Column 5 gives the number of persons who may risk to die in the interval concerned. For the interval 0–1 year there were no surviving patients in column 3 and all 192 persons were thus exposed to death during the whole of the interval. In the next year 1 person is left out as surviving and it is then a general statistical rule to assume that this person will be exposed to death during the half of the interval for which reason the number of person years exposed to death during the interval is 160.5. In the interval 4–5 10 persons are left out the number of surviving persons at the beginning of the interval 116 is therefore reduced by $\frac{10}{2}$ to 111.

Column 6 gives the probability of death calculated as the ratio between the number of deaths in the interval (column 2) and the number of person years exposed to death (column 5). For the interval 0–1 year 31/192 = 0.161.

Column 7 states the survival percentage for the interval. It therefore begins with 100. Of these a fraction of 0.161 will die in the course of the first interval thus 16.1 per cent of the chosen 100 per cent. There remains then after the first interval 100 − 16.1 = 83.9 per cent. Of these a fraction of 0.093 or 83.9 by 0.093 = 7.8 per cent will die in the course of the interval 1–2 years. This leaves 83.9 − 7.8 = 76.1 per cent and so on.

The results in column 7 are plotted in a survival curve on semilogarithmic paper. For the purpose of estimating the survival this curve is supplemented several times in the following by a survival curve for a corresponding age group calculated from the survival of the average population according to the data given in *Statistisk Årbog for Danmark* (Statistical Yearbook for Denmark) vol 52 Table 23 1947. The experiences of normal mortality used are of the years 1941 to 1945 which cover the middle of the period comprised by the period of observation of the series. It may be mentioned that according to *Berkson* a calculation has been used from the average age of the series of patients at the beginning of the interval.

The use of the *indirect* (or actuarial) method in calculations of survival in the present series of cases was necessitated by the highly varying period of observation. It must however be pointed out that according to *Berkson's* experiences the *direct* method in which the survival is determined after a definite period e.g. 10 years gives practically the same results as the method used here (*Berkson and Gage* 1950).

With the technique used here the (arithmetical) *average duration of life* or *average survival time* of the whole series cannot be stated since as already mentioned this value is known only in the case of patients who died. The (arithmetical) average survival time can however be given for the dead pa

tients separately and for the living patients at the time of the follow up separately In some of the following chapters these values are used for comparison with the findings in the literature

With regard to the total series however the *median survival time* can be given This is the period required for 50 per cent of the individuals to have died The median survival time can be directly read from the survival curve by noting the place on the time scale corresponding to where the curve crosses the 50 per cent level

Chapter IV

Isolated Mitral Stenosis

In this chapter the clinical picture of isolated mitral stenosis and a survey of its course will be given on the basis of the writer s series of cases

Composition of the series

The series comprise 271 patients 261 patients have been included owing to the fact that the clinical diagnosis of isolated mitral stenosis had been estab lished at the first observation and 10 patients have been included solely on the basis of the autopsy diagnosis isolated mitral stenosis

The safety of the clinical diagnosis of isolated mitral stenosis was discussed on page 39 where it was pointed out that all clinical diagnoses established were verified in 75 cases at autopsy and in 78 cases subjected to follow up examination Furthermore it was mentioned on page 33 that in 12 out of 78 cases with the diagnosis of isolated mitral stenosis at the first observation the presence of complicating aortic disease was ascertained at the follow up

In 108 cases in all of the present series (104 patients who died without being autopsied and 4 who were not followed up) the diagnosis of isolated mitral stenosis could not be verified later and thus a thoroughly sharp distinction between *isolated mitral stenosis and combined mitral stenosis and aortic* disease cannot be carried through It was therefore decided to use the clinical diagnosis at the first observation as a basis of classification and consequently there is a low proportion of cases with complicating aortic disease in the series thus defined

Findings at the first clinical examination of the heart

In 261 out of the 271 patients the diagnosis has been clinched by the finding of characteristic diastolic and/or presystolic apical murmurs In 130 cases the murmurs affording the diagnosis had been described as chiefly diastolic in 67 cases as chiefly presystolic and in 64 cases as diastolic and presystolic murmurs i e occupying the whole diastole

An unquestionable mitral snap has been described in 61 patients and a dis tinctly accentuated 1st sound has been mentioned in 79 patients However the information about these two signs was not considered complete

Systolic apical murmurs have been described in 107 patients (40 per cent)

These systolic murmurs have not been graduated in detail with regard to intensity or duration

Mitral incompetence in the series – Owing to the presence of these systolic murmurs the question naturally arises how often an organic component of mitral incompetence may have been present in this series The question cannot be answered with certainty but on the basis of the experiences previously mentioned with regard to surgical verification of the clinical diagnoses of mitral disease (see page 14) it must be assumed that the series of isolated mitral stenoses as defined here must include a number of patients with a component of regurgitation Considering the experience from this hospital mentioned on page 14 it must be estimated that about one sixth of the 154 patients without systolic murmurs have had a predominant mitral stenosis with some degree of incompetence (26 patients) and that about one third of the 107 patients with combined diastolic presystolic and systolic murmurs (36 patients) have had predominant stenosis with some degree of incompetence According to this estimate a total of 62 out of 261 cases diagnosed at clinical examination of the heart or about 24 per cent may thus have had a component of regurgitation associated with predominant mitral stenosis

In the case of predominant mitral incompetence with slight stenosis the incidence in the mentioned surgical series was found to be one third of patients with systolic murmurs and provided the assumption holds good it should be about 36 cases in all or 14 per cent of the series thus a low proportion The estimate mentioned is of course beset with considerable uncertainty but it can hardly be very wrong to consider the present series of cases as one of mitral disease with pure or predominant stenosis in the great majority of cases

SURVEY OF THE SERIES AT THE FIRST OBSERVATION

The following is a survey of the series of cases of isolated mitral stenosis forming an introduction to the next sections in which the separate problems will be dealt with in greater detail

Sex incidence – *The series comprises 194 females and 77 males There is* thus a great majority of females The ratio females males is 2 5 1

This sex incidence is in accord with the findings in most series of cases of isolated mitral stenosis reported in the literature *Nylin* (1952) in a Swedish series thus found the ratio 2 4 1 between females and males In an English series *Jones* (1933) found the ratio 2 8 1 and in two series of the U S A *Willius* (1927) and *Levine and Fulton* (1928) gave the ratios 2 1 1 and 2 2 1 In *Aastrup* s Danish series there was a somewhat lower majority of females (1 5 1)

whereas *Biorck et al* (1951) recently found the ratio 4 4 1 in a Swedish series

Age incidence – The ages at the first observation varied from 14 to 73 years The average age for the whole series is 41 5 years The average age for females is 41 6 years and for males 41 4 years

It appears from Fig 2 which shows the age and sex incidence in the series that the series is one of adult patients There are only 8 patients under 20 years and only 35 patients in the age group 20–29 years The age groups 30–39 years and 40–49 years with 80 and 78 patients respectively constitute the greater part of the series But there are 70 in all over 50 years including 16 over 60 years and 2 over 70 years Thus a total of 70 out of 271 patients were over 50 years (26 per cent) at the first examination

As already mentioned males and females have the same average age It appears from Fig 2 that the female majority is to be found especially in the age groups between 30 and 50 years

The average age 41 6 years at the first observation in the present series is 10 years higher than that in *Grant* s series of servicemen (1933) and accordingly only 4 per cent of the patients were in the age groups over 50 years in the latter series as compared to 26 per cent in the present one The average age in the present series is also higher than those given in the series reported by *Jones Willius Levine and Fulton* and *Aastrup* in which the incidences of patients over 50 years of age are 5 9 12 and 16 per cent respectively *Nylin* s series with 23 per cent of the patients at ages over 50 resembles the present series most in this respect Only the series reported by *Biorck et al* has a higher average age with 45 per cent over 50 years as compared to 26 per cent in the present series

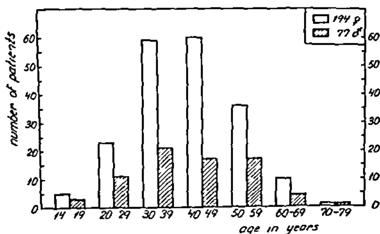


Fig 2
Age and sex incidence of isolated mitral stenosis at first observation

The latter thus contains a greater number of elderly patients than do most other series of cases of isolated mitral stenosis reported in the literature

Rheumatic infection – Information about a past history of rheumatic infection was available in 159 out of 271 patients (58 [illegible] per cent)

Rheumatic fever only had been present in 132 cases chorea minor in 11 rheumatic fever plus chorea minor in 10 and scarlatinal rheumatoid arthritis in 3 cases In 112 cases the past history did not definitely suggest a clinically recognized acute rheumatic infection 21 of these patients stated that they had been suffering from recurrent acute tonsillitis 5 had had a severe tonsillitis or a tonsillar abscess 7 had had unclassifiable fevers and 1 patient had had erythema nodosum

Rheumatic recurrences were present in 87 out of the 159 patients with a past history of rheumatic infection The percentage of recurrences in the present series is thus 55

The average age at the first rheumatic infection was 15 4 years The average interval between the first rheumatic infection and the first observation was 25 4 years Further details about the placing of the rheumatic infection in the course of the disease will be given in the section on the rheumatic infection

Duration of symptoms – The great majority of the patients had had cardiac or circulatory symptoms for a prolonged time before the first observation In the present work importance was attached to an investigation of the consequence of age when the first symptom appeared and the present series of cases shows the age incidence given in Table 5

TABLE

194 Females and Males with Isolated Mitral Stenosis Distributed according to Age when First Heart Symptoms appeared

Age group	Females	Males	Total		Cumulative
[illegible]–9 years	10		1	4	4
10–19	34	14	48	18	[illegible]
[illegible]0–[illegible]9	44	18	6	[illegible]3	4
30–39	57	13	0	26	71
40–4[illegible]	28	15	43	16	87
50–59	15	13	[illegible]5	10	97
60–69	3	1	4	1 [illegible]	98 [illegible]
no information available	3	1	4	1 5	100
	194	[illegible]	271	100	100

Table 5 shows that 4 per cent of the series have had symptoms before the tenth year that 22 per cent of the patients have had cardiac or circulatory symptoms before the twentieth year 45 per cent before the thirtieth year 71 per cent before the fortieth year and 87 per cent before the fiftieth year whereas 11 5 per cent developed symptoms later The age when the first symptoms appeared has not been ascertained in 4 cases (1 5 per cent)

The average age when the first symptom appeared was 31 2 years and the average duration of the symptoms at the first observation was 10 3 years

Nature of first symptom

TABLE 6

Nature of First Symptom in 271 Cases of Isolated Mitral Stenosis

Symptom	Number of patients
Dyspnoea	224
Palpitation	26
Precordial pain	1
Dizziness	1
Premature beats	2
Paroxysmal tachycardia	1
Paroxysmal auricular fibrillation	2
Chronic auricular fibrillation	3
Acute pulmonary oedema	1
Haemoptysis	4
Pulmonary embolism	4
Arterial embolism	2
Total	271

It appears from Table 6 in which the series of isolated mitral stenoses is grouped according to the most important first symptom that dyspnoea was the first symptom in 224 out of 271 patients (83 per cent) 26 patients stated that the disease had set on with palpitation in 1 patient it had set on with precordial pain in 1 with dizziness in 2 with premature beats in 1 with paroxysmal tachycardia in 2 patients with paroxysmal auricular fibrillation in 3 with chronic auricular fibrillation in 1 with acute pulmonary oedema in 4 with haemoptysis in 4 with pulmonary embolism and in 2 patients with arterial embolism

A detailed analysis of the single symptoms will not be given in this connection as the conspicuous symptoms will be dealt with in the various sections

on symptoms in the following Only the frequency of some special clinical symptoms may be mentioned

Special clinical symptoms

Acute pulmonary oedema plus cardiac asthma occurred in 27 patients (10 per cent of the cases)

Haemoptyses were present in 36 patients in all (13 per cent of the cases) In this group haemoptyses occurred in 11 patients in conjunction with acute pulmonary oedema and cardiac asthma or alternating with these symptoms and in 2 patients the haemoptyses occurred in conjunction with pulmonary embolism Haemoptyses that could not be related to cardiac asthma and acute pulmonary oedema or pulmonary embolism occurred in 23 patients

Pulmonary embolism was present in 16 patients (6 per cent of the cases)

Arterial embolism occurred in 29 patients (11 per cent of the cases)

Among other special symptoms mention may be made of the following –

Pneumonia had been present in 44 patients (16 per cent of the series) In addition there were many cases of bronchitis and catarrhal affections

Premature beats with a characteristic description in the past history of intermittence of normal beats or a fluttering sensation occurred in 32 patients (12 per cent of the cases) The presence of the symptom was verified by electrocardiography in 18 of these patients

Paroxysmal tachycardia or auricular fibrillation was described in 15 patients (6 per cent) In 6 of these cases the diagnosis of paroxysmal auricular fibrillation has been verified by electrocardiography and in 2 cases a paroxysmal tachycardia of supraventricular type has been demonstrated

Precordial pain was a frequent symptom In most cases it was in the form of stinging pain at the apex beat in some it was a sensation of oppression behind the sternum in conjunction with the dyspnoea on exertion Pain bearing a close resemblance to true angina pectoris has been described in 11 patients (4 per cent of the cases) Cardiac infarction verified at electrocardiography had been previously described in 2 of these cases One was a man aged 69 with anterior wall infarction the other a woman aged 49 with posterior wall infarction Of the remaining 9 patients 8 were females and 1 was a male 6 patients were over 50 years 5 patients had a normal electrocardiogram and 4 had an iso electric T_1 Only one patient had arterial hypertension

Syncopes have been described in 13 patients (5 per cent of the cases)

Paresis of the recurrent nerve was ascertained in 2 out of 48 patients examined but this is hardly indicative of the incidence of paresis of the recurrent nerve in the series as undoubtedly only specially selected patients have been examined with a view to this complication

Age when diagnosis was first established

A statement of the age when the diagnosis of mitral stenosis was first established would have been of considerable interest but unfortunately this point could not be satisfactorily elucidated in the present series

The Cardiac State

In the description of the series of cases as it appeared at the first examination special importance was attached to providing a picture of the components in the state of the heart which have formed the basis of assessment of the prognosis in isolated mitral stenosis both in the literature and in the writer s series In the following the occurrence of auricular fibrillation and of right ventricular failure in the series will be described besides a survey will be given of the distribution of the series according to the size of the heart and according to the classification with regard to physical activity recommended by the American Heart Association The correlations between these stigmata are mentioned

Heart rhythm at first observation

Auricular fibrillation was present in 155 patients at the first observation (57 per cent) 6 of these had paroxysmal auricular fibrillation whereas 149 had chronic auricular fibrillation Sinus rhythm was found in 116 patients (43 per cent) Electrocardiography had been performed in all cases

TABLE 7

Incidence of Auricular Fibrillation in Relation to Age at First Observation

Age group	Number of patients	Auricular fibrillation patients	
under 19 years	8	2	25
20–29 years	35	13	37
30–39	80	34	43
40–49	78	46	59
50–59	54	45	83
60–69	14	13	93
70–79	2	2	100
Total	271	155	57

Table 7 shows that there is a distinct relation between the incidence of auricular fibrillation and age at the first observation It was present in 25 per cent

in the age group under 19 years in 37 per cent between 20 and 29 years in 43 per cent between 30 and 39 years in 59 per cent between 40 and 49 in 83 per cent between 50 and 59 in 93 per cent between 60 and 69 and in 100 per cent of the patients between 70 and 79 years

The average age of patients with sinus rhythm is 36 4 years and of patients with auricular fibrillation 45 6 years

A detailed survey of the incidence of auricular fibrillation and its relation to age in the series of isolated mitral stenosis reported in the literature has been given by *Aastrup* and the findings in the present series of cases are in close conformity with *Aastrup's* statements

Right heart failure

According to the criteria mentioned on page 43 the presence of right heart failure was ascertained at the first observation in 67 out of 271 patients or in 25 per cent The average age of patients with right heart failure is 45 3 years as compared to 40 7 years in the case of patients without manifest right heart failure As was to be expected the incidence of right heart failure increases with advancing age

Right heart failure frequently occurred in conjunction with auricular fibrillation as shown in Table 8

TABLE 8

Relation between Right Heart Failure and Heart Rhythm

	S h thm		A l f br ll t		T t l
	N mb f p t t	%	N mbe f p t e t	%	
With right heart failure	12	18	55	82	67
Without right heart failure	104	51	100	49	204
Total	116		155		271

At the first observation right heart failure was thus associated with auricular fibrillation in 55 out of 67 patients (82 per cent) whereas it was associated with sinus rhythm in only 12 patients (18 per cent) Of the patients without demonstrated right heart failure 104 had sinus rhythm (51 per cent) whereas 100 had auricular fibrillation (49 per cent)

e of heart

As previously mentioned the cardio thoracic index was used to indicate the e of the heart for the purpose of the present work reference may be made page 36 where the principles used are mentioned Usable roentgenograms re available in 251 out of the 271 cases and a study of these formed the sis of this analysis

A total survey of the whole series examined with regard to the size of the rdio thoracic index is given in Fig 3 showing the index in females and males parately In the case of the women the cardio thoracic index varied from 39 81 There was a total of 23 patients with an index under 50 87 patients with index between 50 and 59 59 patients with an index between 60 and 69 d 12 patients in whom the index was 70 or more In the series of women e mean value of the cardio thoracic index was about 58

In the case of the males 16 patients had a cardio thoracic index below 50 40 it was between 50 and 59 in 10 between 60 and 69 and 4 patients had cardio thoracic index of 70 or more In the male series the mean value of e cardio thoracic index was about 55

It appears distinctly that the male cardio thoracic indices in Fig 3 are largely splaced to the left in relation to those of the women Since judging from e other criteria the men were not in a less advanced phase of the disease an the women this difference must presumably be explained chiefly from e fact mentioned on page 39 that normally the cardio thoracic index de-

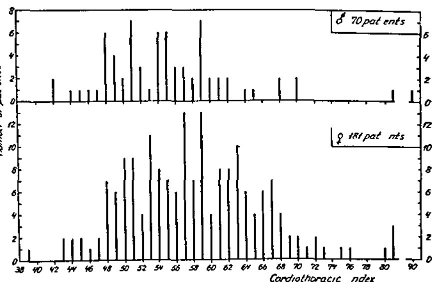


Fig 3

Cardio thoracic index in 251 pat ents with isolated mitral stenos s

creases with increasing width of the thorax This means that the limits between normal and definitely pathological values of the cardio thoracic index must be considered lower in males with their greater width of the thorax than in females

The relation between the cardio thoracic index and manifest right heart failure is demonstrated in Fig 4 In the case of women it shows that the cardio-thoracic index in 44 women with right heart failure was between 51 and 85 with a maximum corresponding to a cardio thoracic index between 61 and 65 In 137 women without right heart failure the index was between 39 and 85, and this group showed a maximum corresponding to a cardio thoracic index between 51 and 55 thus much lower than that of the group with manifest right heart failure It may be mentioned in particular that while the group without manifest right heart failure shows all degrees of cardio thoracic index the group with manifest right heart failure includes only one patient with an index below 56 in all other cases with right heart failure the cardio thoracic index was over 55

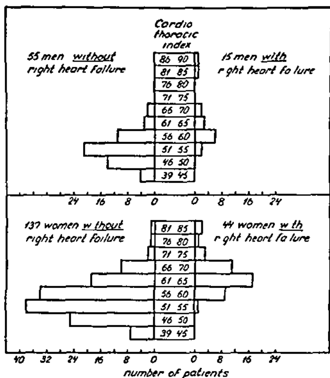


Fig 4
Right heart failure in relation to cardio thoracic index in isolated mitral stenosis

Fig 4 also shows the relation between right heart failure and cardio thoracic index in males 55 without right heart failure had a cardio thoracic index between 39 and 70 with a maximum at values from 51 to 55 15 males with right heart failure had an index between 51 and 90 with a maximum at values from 56 to 60 As was the case in the female patients the males without right heart failure showed all degrees of cardio thoracic index except the very highest whereas only 2 of the male patients with right heart failure had an index below 56 the others being over 55

It was thus found in either sex that right heart failure is almost always associated with a cardio thoracic index over 55

The relation between auricular fibrillation and the cardio thoracic index appears from Fig 5 which shows the cardio thoracic index in sinus rhythm and in auricular fibrillation in 181 women In the group with sinus rhythm comprising 83 women the cardio thoracic index varied between 39 and 70 with a maximum at values from 51 to 55 In 98 patients with auricular fibrillation the cardio thoracic index varied between 39 and 85 and this group showed a maximum between indices of from 56 to 60 In most of the cases with auricular fibrillation the cardio thoracic indices were thus higher than in patients with sinus rhythm It may be mentioned in particular that auricular fibrillation was present with a cardio thoracic index under 51 in only 4 cases and with an index under 56 in only 14 cases whereas the rest of the patients with auricular fibrillation showed higher indices

In the case of males Fig 5 shows that 27 with sinus rhythm had cardio thoracic indices between 40 and 66 with a maximum at values from 46 to 50 whereas 43 males with auricular fibrillation had cardio thoracic indices between 50 and 90 with a maximum at values from 51 to 55 thus a higher average cardio thoracic index than that of the patients with sinus rhythm Only 2 males with auricular fibrillation had a cardio thoracic index under 51 But when the cardio thoracic index exceeds 50 the incidence of auricular fibrillation increases much the maximum being between 51 and 55

Thus it appears that the two sexes show the same tendency to larger hearts in the case of auricular fibrillation than in sinus rhythm The incidence of fibrillation increases much in women with a cardio thoracic index over 54 whereas the increasing frequency of fibrillation in men appears already at an index over 50

In a survey of 200 cases of isolated mitral stenosis *Nylin* has reported exactly the same observations of the relation between the size of the heart and auricular fibrillation and of the relation between the size of the heart and right heart failure Only 7 out of 63 patients with right heart failure in *Nylin*s

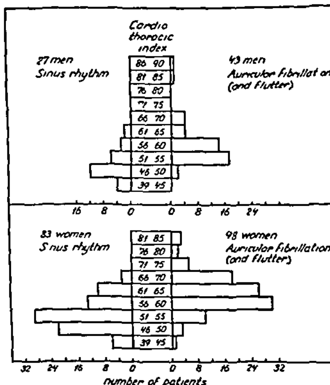


Fig 5
Heart rhythm in relation to cardio thoracic index in isolated mitral stenosis

series had a heart volume under the chosen upper limit of the normal (500 ml per m body surface) and the average heart volume in all cases with right heart failure was much higher than that found in patients without right heart failure Over half of the latter patients had enlargement of the heart Among 99 patients with auricular fibrillation in *Nylin*'s series only 3 had a heart volume under the chosen normal limit The average heart volume in all patients with auricular fibrillation was much higher than that found in patients with sinus rhythm Over half of the latter patients had enlargement of the heart

It seems justifiable to conclude from these observations that the development of the complete heart failure described from the three stigmata heart size heart rhythm and right heart failure generally occurs in such a way that the heart first increases in size then auricular fibrillation develops and this is followed at last by right heart failure

Classification according to physical activity

In conformity with the criteria mentioned on page 44 the series of isolated mitral stenoses at the first observation has been divided by the writer into classes according to the limitation of physical activity As all were cases of mitral stenoses giving rise to symptoms at ordinary physical activity Class I is not represented in the series

TABLE 9

Isolated Mitral Stenoses Classified According to Physical Activity

Cl	M l	F m l	T t l	R l t
I	0	0	0	0
II	18	40	58	21
III	43	116	159	59
IV	16	38	54	20
Total	77	194	271	100

The classification of the series according to limitation of physical activity is given in Table 9 which shows that 58 patients or 21 per cent of the series belonged to Class II 159 or 59 per cent to Class III and 54 or ?0 per cent to Class IV

This distribution is practically the same in males and females

The relation of this classification to age at the first observation was exam ined it appeared that the average age of patients in Class II was 35 2 years in Class III 43 ? years and in Class IV 44 5 years

Correlation between physical activity and heart rhythm

The correlation between physical activity and heart rhythm is shown in Table 10

Table 10 shows that the incidence of auricular fibrillation in males was 56 per cent in Class II 63 per cent in Class III and 75 per cent in Class IV In the ca e of the females the incidence of auricular fibrillation increased from 25 per cent in Class II to 57 per cent in Class III and 79 per cent in Class IV There was thus a distinct tendency to an increasing incidence of auricular fibrillation with increasing limitation of the physical activity The whole series included 35 per cent with auricular fibrillation in Class II 59 per cent in Class III and 78 per cent in Class IV

TABLE 10
Correlation between Physical Activity and Heart Rhythm

	Class II		Class III		Class IV	
	Male	Females	Male	Female	Male	Female
Total number	18	40	43	116	16	38
Cases with auricular fibrillation	10	10	[illegible]	66	12	30
Per cent with auricular fibrillation	56		63	57	75	9
Average percentage	35		59		78	

Correlation between physical activity and right heart failure

The incidence of right heart failure in relation to physical activity is shown in Table 11

TABLE 11
Right Heart Failure in Relation to Physical Activity

	Class II		Class III		Class IV	
	Male	Female	Male	Female	Male	Female
Total number	18	40	43	116	16	38
Cases with right heart failure	0	0	3	19	14	31
Per cent with right heart failure	0	0	7	16	88	82

Of patients with right heart failure at the first observation 3 males and 19 females were in Class III while 14 males and 31 females belonged to Class IV Thus a total of 22 patients out of 67 with right heart failure were in Class III (33 per cent) while 45 belonged to Class IV (67 per cent) Table 11 further shows that there were no cases of right heart failure in Class II that right heart failure was found in 3 out of 43 males and in 19 out of 116 females in Class III (7 per cent and 16 per cent respectively average 13 per cent) and that right heart failure was ascertained in 14 out of 16 males and in 31 out of

38 females in Class IV (88 per cent and 82 per cent respectively average 83 per cent)

Thus it appears that the great majority of patients with right heart failure have been placed in Class IV whereas only a low proportion belong to Class III

Correlation between physical activity and heart si e

To illustrate the relation between physical activity and heart size it was decided to divide the cardio thoracic indices into groups Index to and including 50 index from 51 to 54 inclusive index from 55 to 64 inclusive and index over 64 For reasons previously mentioned suggesting that the index values have a somewhat different significance in the two sexes males and females have been classed separately The relation between cardio thoracic index and physical activity is shown in Table 12

TABLE 12

Correlation between Heart Si e and Degree of Physical Activity

H 1S	M l			F m l		
Ca d th d	Cl			Cl		
	II	III	IV	II	III	IV
under 51	7	11	0	15	16	1
51–54	5	11	1	8	24	0
55–64	6	15	7	13	56	13
65 and more	0	9	5	3	16	16
no data available	0	4	3	1	4	8
Total	18	43	16	40	116	38

Table 12 shows that the highest relative frequency of the two lowest index groups is found in Class II even though the index groups over 55 are also represented in this class In Class III all degrees of cardio thoracic index are represented fairly equally In Class IV almost all cardio thoracic indices are over 55 Increasing limitation of the physical activity is thus generally associated with increasing size of the heart

Correlation between heart rhythm heart si e and degree of physical activity – This appears from Table 13 which shows the total series of isolated mitral stenoses in males and females separately

TABLE 13

Correlation between Heart Rhythm Heart Si e and Degree of Physical Activity

Cardio thoracic index	Males Class						Females Class					
	II		III		IV		II		III		IV	
	SR	AF	SR	AF	SR	AF	SR	AF	SR	AF	SR	AF
under 51	7	0	9	2	0	0	14	1	14	2	0	1
51–54	1	4	4	7	0	1	8	0	17	7	0	0
55–64	0	6	2	13	4	3	6	7	15	41	4	9
65 and more	0	0	0	2	0	5	1	2	2	14	2	14
no data available	0	0	1	3	0	3	1	0	2	2	2	6
Total	8	10	16	27	4	12	30	10	50	66	8	30

SR = sinus rhythm
AF = auricular fibrillation

Table 13 shows that the males in Class II comprise 8 patients with sinus rhythm 7 with cardio thoracic indices under 51 and 1 with an index between 51 and 54 and 10 patients with auricular fibrillation 4 with cardio thoracic indices between 51 and 54 and 6 with indices between 55 and 64

In Class II 30 females had sinus rhythm 14 of these showed cardio thoracic indices under 51 8 had indices between 51 and 54 6 showed values between 55 and 64 1 had a cardio thoracic index *over 65 and in 1 case the size of the* heart had not been stated 10 patients had auricular fibrillation and one of these had a cardio thoracic index under 51 7 were between 5 and 64 and 2 showed indices over 65

In Class III 16 males had sinus rhythm 9 of these had cardio thoracic indices under 51 4 showed values between 51 and 54 and 2 had indices between 55 and 64 2 males had auricular fibrillation 2 with cardio thoracic indices under 51 7 between 51 and 54 13 between 55 and 64 and with indices over 65 the size of the heart had not been stated in 3 cases

Among the females in Class III there were with sinus rhythm 14 had cardio thoracic indices under 51 17 showed values between 51 and 54 15 between 55 and 64 2 had cardio thoracic indic and in 2 cases the size of the heart had not been stated Among III with auricular d cardio thoracic indices un ed values between en 55 and 64 14 had d in 2 cases n he size of the heart were 4 males with with cardio-thoracic and 12 fibrillation

the latter 1 had a cardio thoracic index between 51 and 54 3 showed values between 55 and 64 5 had cardio thoracic indices over 65 and in 3 cases nothing was stated about the index

Eight out of 38 females in Class IV had sinus rhythm 4 with cardio thoracic indices between 55 and 64 2 with indices over 65 whereas no data were available in 2 cases 30 females had auricular fibrillation in 1 of these cases the cardio thoracic index was under 51 9 showed values between 55 and 64 14 were over 65 and in 6 cases the index had not been stated

Summing up it can be ascertained that a classification of the series according to degrees of physical activity decidedly splits up the series in contrast with all other classifications based solely upon heart rhythm and cardio thoracic index As was to be expected such classification however suggests that patients with sinus rhythm and with lower degrees of cardio thoracic index are distributed between Classes II and III whereas those with auricular fibrillation and with higher degrees of cardio thoracic index belong to Classes III and IV

Other Roentgenologic Findings

In dealing with changes in the shape of the heart in the present series a distinction should be made between the series of 58 patients examined orthodiagraphically by *Warburg* and the group of 193 patients examined by teleroentgenography

The criteria on the basis of which the changes in the shape of the heart have been assessed have been previously mentioned on page 40

Roentgenograms

To illustrate the degree to which the roentgen examination in the present series was contributory to the clinical diagnosis of mitral stenosis the part of the series examined by teleroentgenography may first be mentioned 66 patients of this group examined in the postero anterior position and in the right anterior oblique position with contrast medium in the oesophagus may be dealt with first A survey of the findings in this group is given in Table 14 in which the series has been divided into groups according to the size of the cardio thoracic index The table gives all unquestionable findings of enlarged left atrium and of a straight left contour of the heart or findings of bulging pulmonary artery Cases in which both findings are lacking have been classified as uncharacteristic

A total of 59 out of the 66 patients examined in the postero anterior position and in the right anterior oblique position had a visible left atrium (89 per cent) 53 out of the 66 patients presented no waist of the heart or had a bulging pulmonary artery (81 per cent) A total of 49 out of 66 had both a visibly

TABLE 14

Roentgenologic Findings in 66 Patients examined in Postero Anterior Position and in the Right Anterior Oblique Position

Card o th a c de	N mber	V s bl l ft atri m	N wa t f h rt o b lg g p lm a tery	U h cterutc
under 51	8	5	4	o
51–54	16	15	13	-
55–64	25	23	21	1
65 and more	17	16	15	-
Total	66	59	53	3
Per cent	100	89	81	4

enlarged left atrium and a straight left contour of the heart (74 per cent) Only 3 patients presented neither of these findings (4 per cent) whereas 9(per cent showed either one or the other and thus a roentgenologic pictur compatible with the clinical diagnosis and contributory to this

Two out of the 3 patients with quite negative roentgenologic findings had cardio thoracic index under 51 In one of these the clinical diagnosis was late verified at autopsy in the other case the left atrium was distinctly visible in the right anterior oblique position at the follow up 4 years later The third patient without enlargement of the left atrium had an index between 55 and 64 and died later without roentgenologic examination or post mortem verification of the diagnosis

The possibility cannot be ignored that in some of the cases with negative findings in the right anterior oblique position the left atrium might have been visualized in the lateral position with contrast medium in the oesophagus the total percentage of cases with enlarged left atrium would thus have been still higher

Summarizing it can however be ascertained that the roentgen examination in the series dealt with here was contributory to the clinical diagnosis as an enlarged left atrium was demonstrated in 89 per cent of the cases or a straight left contour of the heart (including bulging of the pulmonary artery) in 81 per cent or either of these findings in 96 per cent of the cases

In the same series the frequency of visible left atrium in the postero anterior position alone was examined and this sign was found in 40 patients (62 per cent.) It is of interest to compare this finding with the frequency of demonstrated enlarged left atrium in the part of the series examined by teleroent

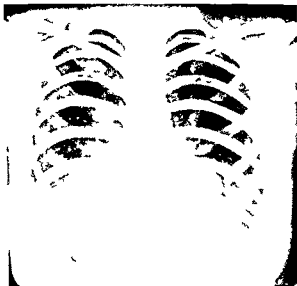




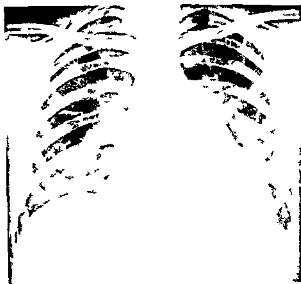
Roentgenogram of l eart and lungs of 8 year old woman with isolated mitral stenos s verified at autopsv At the top the right anterior obl que position with enlarged left atrium making the characteristic impress on in the oesophageal contrast medium At the bottom the bulging second left arch and the left atrium shining through the right frontal contour of the heart Distinctly increased hilar markings



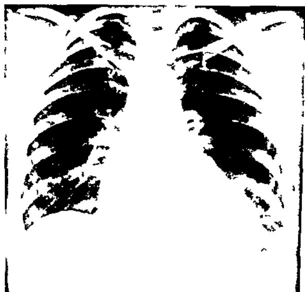
Roentgenogram of heart and lungs – At the top the straight left contour of the heart The width of the heart is normal The picture below shows the same patient 17 years later the width of the heart is distinctly increased and there is distinct bulging of the left atrium on the left border of the heart Distinctly increased hilar markings When last examined the patient was 41 years old and had a clinically isolated mitral stenosis



Roent eno_gram of heart and lungs – Heart much enlarged to the right with characteristic rounded contour Autopsy showed that the r ght contour of the heart was formed by a much dilated left atrium The patient had isolated mitral stenosis



Roentgeno_gram of heart and lungs – Width of heart increased w th bulging of second left arch D stinctly increased hilar markings Autopsy showed isolated mitral stenosis



Roentgenogram of heart and lungs Patient with mitral stenosis combined with aortic valvular disease verified at autopsy There is a distinct increase in the width of the heart with enlarged and elongated left lower arch The left atrium can be seen in the upper right contour

genography in the postero anterior position only This part of the series com prises 127 patients and a survey of these is shown in Table 15

TABLE 15

Roentgenologic Findings in 1°7 Patients examined in Postero Anterior Position only

C d th d	N mb	V bl l ft t m	N w t f h t b lg g p lm t ry	U h t t
under 51	24	13	19	4
51–54	19	11	14	4
55–64	65	47	56	4
65 and more	19	14	13	–
Total	1°7	85	10°	1°
Per cent	100	67	8°	10

Table 15 shows the cardio thoracic index in relation to the finding of en larged left atrium and absence of the waist of the heart (including bulging of the pulmonary artery) and the frequency of uncharacteristic shape in the series examined by teleroentgenography in the postero anterior position only It appears that a visible left atrium was found in 85 out of 127 patients (67 per cent) and that absence of the waist of the heart (including bulging of the pulmonary artery) was ascertained in 102 patients (82 per cent) 12 patients (10 per cent) showed neither of these signs

It may be pointed out that the finding of an enlarged left atrium in 67 per cent is in good conformity with the above mentioned finding of 62 per cent in the postero anterior position alone in the part of the series also examined in the right anterior oblique position The 82 per cent with absence of the waist of the heart corresponds to 80 per cent in the series examined in the right anterior oblique position

In the part of the series examined by teleroentgenography in the postero anterior position alone the clinical diagnosis could thus be verified by the finding of an enlarged left atrium in 67 per cent of the cases by absence of the waist of the heart (including bulging of the pulmonary artery) in 85 per cent of the cases and by either of these signs in 90 per cent whereas this form of roentgen examination was non contributory in 10 per cent of the cases

Orthodiagrams

The series examined by orthodiagraphy comprises 58 patients shown in Table 16

TABLE 16

Roentgenologic Findings in 58 Patients examined by Orthodiagraphy

Ca[illegible] th[illegible] c[illegible] [illegible]dex	N[illegible]mbe[illegible]	[illegible]	[illegible]	U[illegible]
under 51	18	11	14	0
51–54	14	9	12	0
55–64	20	14	16	0
65 and more	6	5	6	0
Total	58	39	48	0
Per cent	100	67	84	0

It may be mentioned that the estimate of the orthodiagraphed series given in Table 16 is based upon the writer s study of the available orthodiagrams This part of the series shows a frequency of definitely demonstrated enlarged left atrium of 67 per cent a frequency of absence of the waist of the heart (including bulging of the pulmonary artery) of 84 per cent and a frequency of either of these signs of 100 per cent In this part of the series the roentgen examination could thus support the clinical diagnosis of mitral stenosis in all cases

That the roentgen examination was thus contributory to the clinical diagnosis of mitral stenosis in the great majority of cases is in accord with the experiences reported by *Warburg* (1932) *Sosman* (1940) and *Nylin* (1952) *Epstein* (1947) has mentioned in particular that definite roentgenologic changes in the shape of the heart may be absent during the early stages of mitral stenosis

Changes in the vascular markings of the lungs

In the absence of definite criteria it was attempted to assess the changes in the vascular markings of the lungs by a mere estimate of the amount of blood and the density of the peripheral lung vessels In the present series this estimate was made on the basis of 189 teleroentgenograms which were usable for this purpose The results are given in the survey below mention may first be made of the hilar markings after which the peripheral vascular markings of the lungs will be dealt with

Of the total series of cases in which the hilar markings were estimated 59 (31 per cent) had normal hilar markings 55 (29 per cent) had doubtfully in

TABLE 1/
Hilar Markings in Isolated Mitral Stenosis

	N rm l h l m k g	D btf lly l h l m k g	D f t ly d h l m k g
Total series number and %	ɔ9 (31)	ɔ (?9)	75 (40)
Number (%) *with* right heart failure	9 (17)	10 (19)	33 (64)
Number (%) *without* right heart failure	50 (37)	45 (33)	4? (30)
Number (%) *with* auricular fibrillat on	31 (?7)	34 (30)	49 (43)
Number (/) *without* auricular f brillation	?8 (37)	?1 (?8)	?6 (35)
Class II Number (%)	14 (4?)	15 (45)	4 (13)
Class III Number (')	37 (34)	3? (28)	43 (38)
Class IV Number (%)	8 (18)	8 (18)	28 (64)

creased hilar markings and 75 patients (40 per cent) presented definitely in creased hilar markings

Table 17 shows that the relation of the hilar markings to such essential findings as right heart failure and auricular fibrillation was examined the relation between the classification according to the degree of physical activity and the hilar markings was also examined

With regard to the patients with right heart failure it appears that 9 (17 per cent) had normal hilar markings 10 (19 per cent) had doubtfully in creased hilar markings and 33 patients (64 per cent) had definitely increased hilar markings In the case of patients without right heart failure there were 50 (37 per cent) with normal hilar markings 45 (33 per cent) with doubtfully increased hilar markings and 42 (30 per cent) with definitely increased hilar markings As was to be expected it thus appears distinctly that right heart failure is most frequently found in conjunction with definitely increased hilar markings

When the series is divided into groups according to heart rhythm it appears that the patients with auricular fibrillation had normal hilar markings in 31 cases (27 per cent) doubtfully increased hilar markings in 34 cases (30 per cent) and definitely increased hilar markings in 49 cases (43 per cent) In the case of sinus rhythm 28 patients (37 per cent) had normal hilar markings 21 (28 per cent) had doubtfully increased hilar markings and 26 (35 per cent) had definitely increased hilar markings Auricular fibrillation is thus apparently associated somewhat oftener with definitely increased hilar markings than is sinus rhythm but the differences are not great

Finally the series has been divided in Table 17 according to the degree of physical activity Among the patients in Class II 14 (42 per cent) have shown normal hilar markings 15 (45 per cent) doubtfully increased hilar markings and 4 patients (13 per cent) have shown definitely increased hilar markings The patients in Class II thus seldom showed definitely increased hilar markings In Class III 37 patients (34 per cent) had normal hilar markings 32 (28 per cent) had doubtfully increased hilar markings and 43 patients (38 per cent presented definitely increased hilar markings thus a fairly even distribution approaching that of the total series In Class IV 8 patients (18 per cent showed normal hilar markings 8 (18 per cent) doubtfully increased and 2 (64 per cent) definitely increased hilar markings The great majority of patients in Class IV thus had definitely increased hilar markings

Summarizing it can be established that the hilar markings as judged in the present series were definitely increased in a great number of the patients who showed signs of more advanced heart disease when judged by other criteria even though definitely increased hilar markings were far from always associated with such other criteria

Vascular markings of the peripheral lung fields

Of the total series of 189 patients 88 had normal vascular markings of the lungs (47 per cent) 42 (22 per cent) showed doubtfully increased vascular markings and 59 (31 per cent) definitely increased vascular markings of the lungs

The relation of the vascular markings of the lungs to right heart failure is given in Table 18 It shows that among patients with right heart failure there were 16 (31 per cent) with normal vascular markings of the lungs 10 (19 per cent) with doubtfully increased and 26 (50 per cent) with definitely increased vascular markings of the lungs Among patients without right heart failure 76 (53 per cent) had normal vascular markings of the lungs 32 (23 per cent) doubtfully increased and 33 (24 per cent) definitely increased vascular markings of the lungs As was to be expected definitely increased vascular markings of the peripheral lung fields are most frequent in cases with right heart failure

Of patients with auricular fibrillation 52 (46 per cent) had normal vascular

markings of the lungs 24 (21 per cent) doubtfully increased and 37 (32 per cent) definitely increased vascular markings of the lungs In the case of sinus rhythm 36 patients (44 per cent) had normal vascular markings of the lungs 18 (24 per cent) doubtfully increased and 22 (29 per cent) definitely increased vascular markings of the lungs In estimating the vascular markings of the peripheral lung fields there was thus no unquestionable difference between patients with auricular fibrillation and such as showed sinus rhythm

TABLE 18

Vascular Markings of the Peripheral Lung Fields in Isolated Mitral Stenosis

	Normal lung markings	Doubtfully increased lung markings	Definitely increased lung markings
Total series number and (%)	88 (47)	42 (22)	59 (31)
Number (%) *with* right heart failure	16 (31)	10 (19)	26 (50)
Number (%) *without* right heart failure	72 (53)	32 (23)	33 (24)
Number (%) *with* auricular fibrillation	5[illegible] (46)	24 ([illegible]1)	37 (32)
Number (%) *without* auricular fibrillation	36 (44)	18 (24)	[illegible] (29)
Class II Number (%)	21 (64)	10 (30)	[illegible] (6)
Class III Number (%)	[illegible]6 (50)	22 (20)	34 (30)
Class IV Number (%)	11 (25)	10 (23)	23 (52)

In Table 18 at the bottom the series has been divided according to degrees of physical activity Of the patients in Class II 21 (64 per cent) had normal vascular markings of the lungs 10 (30 per cent.) had doubtfully increased and 2 (6 per cent) definitely increased vascular markings Thus the patients in Class II had almost always normal or doubtfully increased vascular markings

of the peripheral lung fields and very seldom definitely increased vascular markings In Class III there were 56 patients (50 per cent) with normal vascular markings 22 (20 per cent) with doubtfully increased and 34 (30 per cent) with definitely increased vascular markings of the lungs thus a fairly even distribution In Class IV 11 patients (25 per cent) had normal vascular markings 10 (23 per cent) had doubtfully increased and 23 (52 per cent) definitely increased vascular markings In Class IV over half the patients thus had definitely increased vascular markings of the lungs

This analysis thus showed that the vascular markings of the peripheral lung fields as estimated in the present series were definitely increased in a great number of patients who had shown signs of more advanced heart disease when judged by other criteria But as in the case of the hilar markings the correlation to such other criteria of advanced heart disease was far from obligatory

Other pulmonary changes

Obliteration of the pleural sinus was found in 11 patients including 8 in whom it was associated with right heart failure and interpreted as hydrothorax and 3 patients in whom it was considered due to pulmonary infarction In another 3 patients infiltrates were found in the lung fields and regarded as pulmonary infaction One patient had a diffuse characteristic haemosiderosis This case will be dealt with later (see page 138)

Electrocardiographic Findings

Auricular fibrillation the most important electrocardiographic finding in mitral stenosis has been previously mentioned The other electrocardiographic findings will be dealt with in this section

One or more electrocardiograms taken with the classic limb leads were available in 269 cases of isolated mitral stenosis and this material forms the basis of the following exposition

Changes in the P waves

As mentioned on page 42 the criteria for abnormal P waves were (1) P wave wider than 0 13 second (2) P_1 taller than 2 0 mm or P taller than 2 5 mm and (3) splitting of the P wave as far as to the iso electric level (or double P wave)

According to these criteria abnormal P waves were found in a total of 34 out of 114 patients with sinus rhythm (30 per cent) The incidence of abnormal findings is shown in Table 19

TABLE 19

P wave Changes in 114 Patients with Sinus Rhythm

Normal P waves	80 patients
Abnormal P waves	34
P waves > 0.13 second	14
P waves abnormally tall	15
P waves abnormally split	10
P waves abnormal according to one criterion	29
P waves abnormal according to several criteria	5

P waves measuring more than 0.13 second in width occurred in 14 cases including 11 without abnormal height or abnormal splitting and in 3 cases combined with abnormal height (2 cases) or abnormal splitting (2 cases).

P waves of definitely increased height occurred in 15 cases including 11 without simultaneous abnormal width or abnormal splitting whereas 4 cases also presented increase of width (2 cases) or abnormal splitting (3 cases).

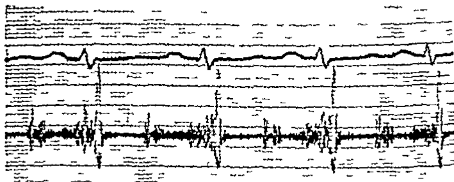
Abnormally split P waves occurred in 10 cases including 6 without simultaneous increase in width or height whereas 4 cases showed abnormal height (3 cases) or abnormal width (2 cases).

According to the chosen criteria pathological P waves were thus found in the writer's series in 34 out of 114 cases of isolated mitral stenosis with sinus rhythm or in 30 per cent. The P wave changes in these cases may be considered contributory to the clinical diagnosis since according to *Larsen and Skulason's* investigations (1941) changes in the P waves of this nature will very seldom be found in normal individuals; furthermore according to the strict criteria used here it may be considered certain that only definitely abnormal P waves will be characterized as pathological.

The literature contains highly varying statements of the frequency of abnormal P waves in mitral stenosis according to the strictness of the criteria used. The investigations from Norway by *Rasmussen and Nyhus* (1948) can best be compared with the present series. These authors used the same criteria and found abnormal P waves in 13 out of 48 cases of mitral stenosis (25 per cent.) including 7 cases with increased width of the P waves, 3 with increased height and 10 with abnormal splitting, the criteria being combined in 7 cases.

Prolongation of the P R interval

In 4 patients out of 114 with sinus rhythm the duration of the P R interval was longer than 0.22 second. In two patients aged 47 and 49 there were



Phonocardiogram from patient with isolated mitral stenosis showing a distinct diastolic presystolic murmur

Electrocardiogram (limb leads) from patient with isolated mitral stenoses Double P_I increased in width Right axis deviation T waves normal

clinical signs of rheumatic recurrence whereas the prolonged P R interval could not be explained in the two other cases

Prolongation of the P R interval was thus a rare finding in the present series (scarcely 4 per cent) This is in accord with the incidence of prolonged P R interval in 4 out of 48 patients in *Rasmussen and Nyhus* s series In an

English series *Trounce* (1952) found prolongation of the P R interval in 4 out of 75 patients with mitral stenosis

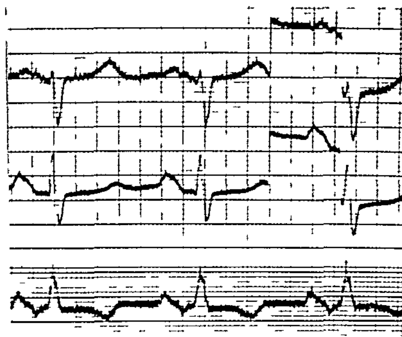
The ventricular complex

In the description of the ventricular complex mention may first be made of the QRS complex and then of the T waves

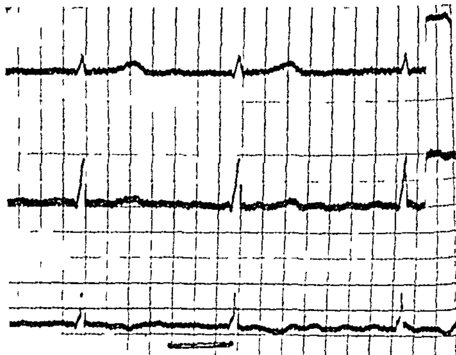
As already mentioned on page 42 *the QRS axis* was determined in every one patient by means of a diagram described by *Wilson and Herrmann* (1920) and divided into 30 degree intervals

In the total series 11 patients (4 per cent) had a QRS axis between +120 and +150 degrees 68 patients (26 per cent) had a QRS axis between +90 and +120 degrees in 91 patients (33 per cent) it was between +60 and +90 in 58 (21 per cent) between +30 and +60 in 32 (12 per cent) between 0 and +30 degrees whereas 9 patients (3 per cent) showed a QRS axis between —30 and 0 degrees In the total series of mitral stenoses 79 patients (29 per cent) thus had a QRS axis to the right of +90 degrees 181 patients (67 per cent) had a QRS axis between 0 and +90 degrees and 9 patients (3 per cent) had a QRS axis to the left of 0 degrees

In 2 out of the last mentioned 9 patients the left axis deviation can be ex



Electrocardiogram (limb leads) from patient with isolated mitral stenosis showing right axis deviation elevated P and negative T_3



Electrocardiogram from patient with isolated mitral stenosis showing auricular fibrillation QRS axis +30 – +60 degrees

plained by the presence of severe arterial hypertension causing both patient to die of cerebral haemorrhage In both cases autopsy showed isolated mitra stenosis and severe cerebral haemorrhage In two other patients of this grou the mitral stenosis was verified at autopsy but complications explaining th *left axis deviation could not be demonstrated here* The *remaining 5 patient* with left axis deviation died later these cases were not autopsied and non had had clinical signs of complicating aortic disease or of arterial hyperten sion Only one had a systolic apical murmur suggesting mitral incompetence In 6 patients with clinically pure mitral stenosis a left axis deviation was thus found which could not with certainty be explained by complicating diseases

The distribution of the present series with 29 per cent in the QRS range to the right of +90 degrees 67 per cent in the range from 0 to +90 degrees and 3 per cent to the left of 0 degrees corresponds to that given in *Rasmussen and Nyhus*s series These authors had 28 per cent with right axis deviation 63 per cent with normal axis and 9 per cent with left axis deviation *Carouso et al* (1950) found 35 per cent with right axis deviation among 206 mitral stenoses and *Nylin* had 32 per cent with right axis deviation in 200 cases of *mitral stenosis*

QRS axis and heart rhythm

TABLE ²0

QRS Axis in Relation to Heart Rhythm in Isolated Mitral Stenosis

QRS	> +90	0 +90	30 – 0
Sinus rhythm	33 (29 %)	79 (69 %)	2 (2 %)
Auricular fibrillation	46 (30 %)	102 (66 %)	7 (5 %)

The table shows that 29 per cent of the patients with sinus rhythm had right axis deviation 69 per cent had a normal axis and 2 per cent had left axis deviation Of the patients with auricular fibrillation 30 per cent had right axis deviation 66 per cent a normal axis and 5 per cent had left axis deviation There was thus no difference in the distribution of the QRS ranges in sinus rhythm and in auricular fibrillation

Changes in the T waves

Estimating from the criteria for T wave changes mentioned on page 13 it was found that 128 out of 269 patients (48 per cent) had normal T waves 56 (21 per cent) had a negative T_3 as the only anomaly 6 patients (2 per cent) had negative T and T_3 as the only T wave change 75 (28 per cent) had an iso electric T_1 with or without other T wave anomalies and 4 patients (1 per cent) had a negative T_1

TABLE 21

T Wave Changes in Relation to QRS Axis

	QRS i th gbt f +90	QRS betw e +90 d 0	QRS b twe 0 d 30
Normal T waves	28	97	3
T_3 negative	23	33	0
T and T_3 negative	1	[illegible]	0
T_1 0	24	49	[illegible]
T_1 negative	0	0	4
Total	79	181	9

Table 21 shows that among 79 patients with right axis deviation normal T waves were found in 28 (35 per cent) a negative T_3 was found in 23 (29 per

cent) negative T and T_3 were seen in 4 (5 per cent.) iso electric T_1 was found in 24 (30 per cent) whereas a negative T_1 was not seen in any of the cases

Among 181 patients with a normal QRS axis 97 (54 per cent) had normal T waves 33 (18 per cent) had a negative T_3 2 (1 per cent) had negative T and T_3 49 (27 per cent) showed an iso electric T_1 with or without other T wave changes whereas a negative T_1 was never seen

Of 9 patients with a QRS axis between 0 and —30 degrees 3 had normal T waves (33 per cent) 2 (22 per cent) showed iso electric T waves and 4 (44 per cent) a negative T_1

There was thus a relatively high incidence of negative T_3 and negative T and T_3 among patients with right axis deviation as compared to patients with a normal QRS axis On the other hand the frequency of iso electric T_1 with or without other T wave changes was almost the same in the two ranges of the axis A negative T_1 was seen only in the case of left axis deviation

If this series is re arranged with a view to heart rhythm and digitalis medication before the examination the distribution is as follows –

TABLE 22

T Wave Changes in Relation to QRS Axis Heart Rhythm and Digitalis Medication

	QRS +90 – +150			QRS 0 +90			QRS –30 0		
	SR	AF		SR	AF		SR	AF	
		+d g	d g		+d g	no d g		+d g	o d g
Normal T waves	18	8	2	56	27	14	1	2	0
T_3 negative	9	11	3	15	15	3	0	0	0
T $_3$ negative	2	2	0	0	2	0	0	0	0
T_1 0	4	15	5	7	27	15	0	2	0
T_1 negative	0	0	0	0	0	0	2	0	2
Total	33	36	10	78	71	32	3	4	2

SR = sinus rhythm
AF = auricular fibrillation

It appears from Table 22 that among the 33 patients in the group with right axis deviation and sinus rhythm 18 (55 per cent) had normal T waves 9 patients (27 per cent) had a negative T_3 2 (6 per cent) had negative T and T_3 and 4 (12 per cent) had an iso electric T_1 Among 36 patients with right axis deviation and auricular fibrillation who had been treated with digitalis 8 (24 per cent) had normal T waves 11 (33 per cent) had a negative T_3 2 (6 per

cent) negative T_2 and T_3 and 15 (44 per cent) had an iso electric T_1 with or without other T wave changes Among 10 patients with right axis deviation and *auricular fibrillation who had not been treated with digitalis* 2 (20 per cent) had normal T waves 3 (30 per cent) had a negative T_3 and 5 (50 per cent) an iso electric T_1

According to the classification used the number of abnormal T waves is thus considerably higher in auricular fibrillation than in the case of sinus rhythm The difference in the frequency of negative T_3 and negative T and T_3 is but slight 33 per cent in all in the case of sinus rhythm as compared to 39 per cent in auricular fibrillation with digitalis treatment and 30 per cent in auricular fibrillation without digitalis treatment In the group with iso electric T_1 (with or without other T wave changes) there is however a distinct difference as there were only 12 per cent in the case of sinus rhythm as compared to 44 per cent and 50 per cent in auricular fibrillation with and without digitalis treatment respectively

In the group with a QRS axis between +90 and 0 degrees 56 out of 78 patients with sinus rhythm had normal T waves (72 per cent) 15 patients (19 per cent) had a negative T_3 7 (9 per cent) an iso electric T_1 Among 71 patients with auricular fibrillation who had received digitalis 27 (32 per cent) had normal T waves 15 (21 per cent) had a negative T_3 2 (3 per cent) negative T and T_3 and 27 (32 per cent) an iso electric T_1 Among 32 with auricular fibrillation not treated with digitalis 14 (44 per cent) had normal T waves 3 (9 per cent) a negative T_3 and 15 (47 per cent) an iso electric T_1

In this group the finding mentioned in the case of right axis deviation recurs that an iso electric T_1 (with or without other T wave changes) is much more *frequent in auricular fibrillation than in sinus rhythm and that there are no* distinct differences between those of the patients with auricular fibrillation that have been treated with digitalis and those who have not

The group with left axis deviation cannot contribute further to this finding

The occurrence of a negative T_3 and negative T and T_3 was thus more frequent in the case of right axis deviation whereas the presence of an iso electric T_1 (with or without other T wave changes) has no definite relation to the QRS axis but a distinct relation to auricular fibrillation and with regard to the occurrence of an iso electric T_1 no unquestionable difference was found between patients with auricular fibrillation who had been treated with digitalis and such as had not been so treated

The T wave changes in relation to the degree of physical activity appear from Table 23 Among 37 patients with sinus rhythm in Class II 29 (78 per cent) had normal T waves 7 (19 per cent) had a negative T_3 and 1 patient an iso electric T_1 (3 per cent) Of 20 patients with auricular fibrillation in Class II 12 (60 per cent) showed normal T waves 1 (5 per cent) a negative

TABLE 23

T Wave Changes in Relation to Degree of Physical Activity

	Class II SR	Class II AF	Class III SR	Class III AF	Class IV SR	Class IV AF
Normal T waves	29	12	42	38	4	3
T_3 negative	7	1	13	21	4	10
T $_3$ negative	0	0	2	2	0	2
T_1 0	1	7	7	31	3	26
T_1 negative	0	0	1	1	1	1
Total	37	20	65	93	12	42
With right axis	4	8	21	20	8	18

(Digitalis treatment has not been considered in this table)

SR = sinus rhythm
AF = auricular fibrillation

T_3 and 7 (35 per cent) an iso electric T_1 Any treatment with digitalis ha not been considered in this connection

Of 65 patients with sinus rhythm in Class III 42 (65 per cent) had norma T waves 13 (20 per cent) a negative T_3 2 patients (3 per cent) showed negative T and T_3 7 (11 per cent) an iso electrictric T_1 and 1 patient (2 per cent) had a negative T_1 Among 93 patients with auricular fibrillation 38 (41 per cent) had normal T waves 21 (22 per cent) had a negative T_3 2 (2 per cent) had negative T and T_3 31 (33 per cent) an iso electric T_1 and 1 patient (1 per cent) had a negative T_1

In Class IV 4 out of 12 patients with sinus rhythm (33 per cent) had normal T waves 4 (33 per cent) a negative T_3 3 (25 per cent) an iso electric T_1 and 1 (8 per cent) a negative T_1 Among 42 patients with auricular fibrillation in Class IV 3 (7 per cent) showed normal T waves 10 (24 per cent) a negative T_3 2 (5 per cent) negative T and T_3 26 (62 per cent) an iso electric T_1 and 1 patient (2 per cent) had a negative T_1

Thus there was no distinct difference in the frequency of negative T_3 and negative T and T_3 in the various groups There was however a distinct rise in the incidence of iso electric T_1 from Class II to Class IV among patients with sinus rhythm and from Class III to Class IV among those with auricular fibrillation

Bundle branch block

An initial complex of a duration exceeding 0 12 second was found in 5 out of 269 patients (2 per cent) In 4 patients all males at ages of 39 54 56 and 59 years it was in the form of right bundle branch block The last patient a woman aged 73 showed a typical left bundle branch block In the series published by *Rasmussen and Nyhus* bundle branch block according to the criteria used here was present in 6 out of 100 patients In the series of *Carouso et al* (1950) bundle branch block was found in 8 out of 206 patients (4 per cent)

Low voltage

This was observed in 2 out of 269 patients (1 per cent) Both were women they were 51 and 62 years of age and both had auricular fibrillation and right heart failure

RESULTS OF FOLLOW UP

This section gives a survey of the series of isolated mitral stenoses as it appeared at the time of the follow up The period of observation varies from 3 to 20 years averaging 12 0 years

The original series comprised 271 patients 189 died (70 per cent) during the period of observation whereas 82 (30 per cent) were alive at the time of the follow up In the following a survey of the dead will first be given after which mention may be made of the survivors as this exposition is to form the basis of the more detailed analysis of the course of mitral stenosis given in the next chapters

SURVEY OF PATIENTS WHO DIED DURING PERIOD OF OBSERVATION

Age at death

The youngest patient died at the age of 14 years the oldest at the age of 78 The distribution of the series according to age at death is shown in Fig 6 which gives the number of deaths for either sex in decades 3 patients died before the 20th year 17 between the 20th and 29th years 37 between the 30th and 39th years 52 between the 40th and 49th years 45 between the 50th and 59th years 30 between the 60th and 69th years and 5 died between the 70th and 78 years

A total of 57 patients (30 per cent) died before the 40th year and 80 (42 per cent) in all after the 50th year

The age at the time of death averages for the whole series 47 0 years for males only 46 1 years and for females only 47 3 years

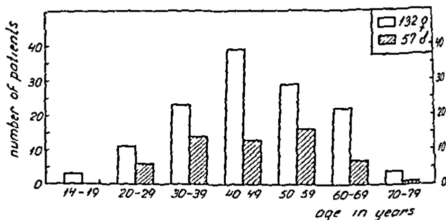


Fig 6
Cases of isolated mitral stenosis arranged according to age at the time of death

The deaths comprised 132 females and 57 males and Fig 6 shows that the female preponderance is highest in the age groups between 40 and 69 years

The average age at death in the present series is higher than in other clinical series of mitral stenosis published in which the patients were followed throughout their lives This appears from Table 24

In clinical series of mitral stenosis followed throughout life the average age at death has been stated to be from 33 years (*DeGraff and Lingg*) to 41 years (*Willius* 1927) and 42 7 years (*Aastrup*) a calculation from *Grant* s table gives an average at death of 40 9 years in his series of enlisted men

When the average ages in clinical series followed throughout life are to be assessed both the age incidence and the severity of the disease in the original series and the length of the period of observation should be considered as mentioned previously on page 45 The reason why *DeGraff and Lingg* found such low figures for the average age at death is undoubtedly first of all that their original series comprised many young and seriously ill patients and comparatively few older patients Furthermore it seems probable that the average age at death would have been found to be higher in the case of a longer period of observation For as already mentioned an analysis after a short period of observation will always comprise the shortest courses of the disease and too few of the more prolonged ones The present series of cases differs from all the above mentioned clinical series of mitral stenosis followed throughout life by having a higher average age and a longer period of observation The finding of a higher average age at death in the present series should therefore undoubtedly be viewed against this background

Compared with the autopsied series of isolated stenoses the present series

TABLE ²4

Age at Death in Mitral St nosis in Clinical Series and in Autopsied Series in the Literature Compared with the Present Series

N t f S d A th	N mb f p t t	A ge ag t d th	P t 50 y
Clinical series observed throughout life –			
Cabot (1914)	116	–	9
DeGraff and Lingg (1934)	40?	33	10
Grant (1933)	100	40)	–
Willius (19?7)	160	41 6	19
Aastrup (1937)	50	4? 7	30
Writer s series	189	47 0	4_
Autopsied series – *Isolated mitral stenoses*			
Cabot (1914)	?00	–	?8
Kiss (1948)	118	–	40
Mitral stenosis and *mitral aortic disease*			
Stone and Feil (1934)	100	Males 4 7 females 38 6	33
Graham *et al* (1951)	101	50 53	58
Rheumatic valvular disease			
Friedberg and Tartakower (1931)	33	53	57

with 42 per cent of deaths after the 50th year is at a higher age level than that of *Cabot* The latter showed 28 per cent of deaths after the 50th year whereas the present series corresponds to that published by *Kiss* who had 40 per cent of deaths after the 50th year (*Kiss* 1948) In the latter 90 per cent of the cases had been clinically recognized In a series of autopsied cases of mitral stenosis and combined mitral and aortic disease *Stone and Feil* (1934) found average ages of 42 7 years for males and 38 6 years in the case of females In a similar series *Graham et al* (1950) found average ages of 50 years for males and 53 years for females They found the same average ages in the cases of isolated mitral stenosis in the series and pointed out that the high average ages were undoubtedly due to the presence in the series of many old cases of mitral stenosis which had not been clinically recognized and had not previously caused appreciable symptoms In *Friedberg and Tartakower* s series

of autopsied cases from Vienna (1931) the average age at the time of death was 53 years This series which included all types of rheumatic valvular disease also contained many elderly patients with valvular disease which had not been clinically recognized It would therefore be expected that such series as the two last mentioned representing a selection of the older part of mitral stenoses would show an average age at death higher than that found in a clinical series for the latter will not often include the benign symptomless cases of mitral stenosis with a long duration of life

Causes of death

A survey of the causes of death is given in Table 25 The classification of the series according to causes of death has been made by the writer in every case after a critical evaluation of all available data It was rather often difficult to establish the actual cause of death since as mentioned especially by *Aastrup* (1937) and by *Juca and White* (1944) there may be several contributory causes In doubtful cases a total estimate of the whole picture was considered to settle the question

Table 25 shows that the causes of death are given in four main groups (1) The main group *heart failure* including congestive failure i e the complete heart failure acute pulmonary oedema sudden death and the group heart death which comprises some less detailed cases died at home owing to the heart disease (2) the main group *thrombo embolic complications* comprising cerebral emboli other arterial emboli in the systemic circulation and pulmonary emboli the main group *infections* comprising active rheumatic infection subacute bacterial endocarditis sepsis and pneumonia and (4) the main group *other causes of death* comprising such causes as suicide cancer tuberculosis leukosis accidents and deaths following surgical operations

The series has been divided into three groups according to the nature of the available information (1) 85 patients died in hospital and autopsied (2) 50 patients died in hospital not autopsied and (3) 54 patients who died in their homes A total of 135 out of 189 patients (71 per cent) thus died in hospital

Table 25 shows that 52 per cent of the autopsied cases died of heart failure 28 per cent of thrombo embolic complications 10 per cent of infections and 10 per cent of other causes of death

Among 50 patients who died in hospital and were not autopsied 67 per cent died of heart failure 18 per cent of thrombo embolic complications 9 per cent of infections and 6 per cent of other causes

Of 54 patients who died in their homes 70 per cent died of heart failure 15 per cent of thrombo embolic complications 9 per cent of infections and 5 per cent of other causes

TABLE 2ɔ

Causes of Death in Isolated Mitral Stenosis

	D d nh p t l t p y	D d h p t l t p y	D d t h m	T t l
Heart failure	*44 = ɔ2 %*	*34 = 6ı %*	*38 = ı0 %*	*116 = 61 %*
1 Congestive failure	4? = 49 %	3? = 64 %	?5 = 47 %	99 = 5 %
2 Acute pulmonary oedema	? = ? %	2 = 4 %	5 = 9 %	9 = 5 %
3 Sudden death	–	–	1 = 2 %	1 = 0 5 %
4 Heart death	–	–	7 = 13 %	7 = 4 %
Thrombo embolic complications	*24 = ?8 %*	*9 = 18 %*	*8 = 15 %*	*41 = ? %*
1 Cerebral emboli	10 = 1? %	5 = 10 %	4 = 7 %	19 = 10 %
2 Other arterial embol	6 = 7 %	1 = 2 %	1 = 2 %	8 = 5 %
3 Pulmonary emboli	8 = 9 %	3 = 7 %	3 = 5 %	14 = %
Infections	*8 = 10 %*	*4 = 9 %*	*ɔ = 9 %*	*17 = 9 %*
1 Active rheumat c fever	3 = 3 %	–	–	3 = 2 %
2 Subacute bact endocarditis	3 = 3 %	–	1 = ? %	4 = 2 %
3 Sepsis	1 = 1 %	2 = 4 %	1 = 2 %	4 = 2 %
4 Pneumonia	1 = 1 %	? = 4 %	3 = 5 %	6 = 3 %
Other causes	*9 = 10 %*	*3 = 6 %*	*3 = ɔ %*	*15 = 8 %*
Total	8	0	54	189

It appears that there is quite a good conformity between the three series with regard to the distribution on the main groups of the causes of death Only there is a somewhat higher percentage of deaths of thrombo embolic complications and a correspondingly lower percentage of heart failures in the autopsied series than in the other groups For practical reasons the series will be dealt with as a whole in the following

In the total series 61 per cent died of heart failure 22 per cent of thrombo embolic complications 9 per cent of infections and 8 per cent of other causes As heart failure thrombo embolic complications and the infections mentioned here must all be considered as belonging to the classic picture of mitral stenosis 92 per cent of the whole series thus died as a consequence of the mitral stenosis and its usual complications

Similarly *Aastrup* found that 44 out of 50 patients with mitral stenosis followed throughout life died of cardiovascular disorders or infections while 6 died of causes other than mitral stenosis and its complications In *DeGraff and Lingg* s clinical series only 10 per cent died of non cardiovascular causes and in *Stone and Feil* s and *Graham et al* s series of autopsied mitral stenoses

(including some with mitral aortic disease) 87 per cent and 93 per cent respectively died of cardiovascular disorders and infections

Deaths of causes without relation to the mitral stenosis amounted to 15 (8 per cent) in the present series of cases 10 women and 5 men The causes of death were 2 cases of suicide 1 case of pulmonary tuberculosis 1 of fibroma of the uterus with necrosis and sepsis 1 of myeloid leukosis 3 cases of cancer (of the pancreas the breast and the pelvic bones) 1 case of collapse under chloroform anaesthesia 2 cases of cerebral haemorrhage (verified at autopsy) and 2 of ileus This group further includes 2 deaths following mitral valvulotomy Three patients of this group had had some degree of right heart failure before they died

Only 3 patients died of unquestionable *rheumatic recurrence* These were women aged 14 22 and 26 in whom the rheumatic recurrence had been clinically diagnosed and verified at autopsy 4 women who died under the picture of septic infection at ages of 31 34 36 and 59 years may possibly have had rheumatic recurrences though no definite signs suggested recurrence Thus only 3 in all out of 189 patients (2 per cent) possibly 7 in all (4 per cent) presented the picture of a fatal clinical rheumatic recurrence in the present series

This analysis was based upon clinical findings The question how often an active rheumatic infection has been contributory to or has directly caused death in the present series cannot be answered definitely Histological examination of the myocardium with a view to rheumatic stigmata has not been made in the series of autopsied cases the frequency of histologically demonstrable rheumatic myocarditis in the series is thus unknown

Apart from cases with definite rheumatic recurrence and such as showed subacute bacterial endocarditis macroscopical *verrucose endocarditis* was present in 12 out of 79 autopsied cases If the verrucose endocarditis is considered indicative of rheumatic activity a total of 15 out of 82 autopsied patients that died with signs of active rheumatic affection (18 per cent) However the justification of interpreting the verrucose endocarditis as a sign of active rheumatic infection in the heart is disputed to some degree For it has been shown by *Gross and Friedberg* (1936) and by *Allen and Sirota* (1944) among others that unspecific thrombo endocarditis without simultaneous histological signs of rheumatic activity in the heart may not infrequently be found also in cases of chronic valvular disease None of these 12 cases with verrucose endocarditis can be recognized from the clinical findings as active rheumatic infections they must thus be considered doubtful in this respect

As already mentioned (see pages 8 and 9) the histological examination of the myocardium in rheumatic valvular disease will reveal signs of rheumatic activity in a much greater number of cases than would be expected when the clinical signs hereof are considered It has been previously emphasized that

the significance of the frequent finding of Aschoff nodules in the myocardium has not yet been fully elucidated the extent to which an active rheumatic infection in the heart contributes to the ultimate heart failure and death is *thus rather doubtful*

Accordingly in series of autopsied cases of rheumatic heart disease the incidence of histological signs of rheumatic activity is highest in the younger age groups In a series of 148 autopsied cases of rheumatic heart disease *Laws and Levine* (1933) thus found 34 cases with signs of rheumatic activity (23 per cent) with an average age of 30 6 years as compared to 37 2 years in the whole series In *Coombs*s series of autopsied cases (1924) the incidence of rheumatic activity during the first four decades was 88 per cent 76 per cent 43 per cent and 33 per cent respectively whereas only 24 per cent of those who died after the 40th year had signs of rheumatic activity In a series published by *Rothschild Kugel and Gross* there were macroscopical or microscopical signs of rheumatic activity in 106 out of 161 autopsied cases of rheumatic heart disease During the first decade in 100 per cent. of 22 in the second decade in 95 per cent *of 44 in the third in 78 per cent of 16 in the fourth in 70 per cent of* 30 in the fifth in 38 per cent of 21 in the sixth in 13 per cent of 15 in the seventh in 12 per cent of 9 and in the eighth decade in 0 per cent. of 4 Heart failure was present in 103 out of the 106 cases with signs of rheumatic activity and Aschoff nodules were found in 95 The authors conclude that the presence of heart failure in cases with valvular disease during the first five decades can be attributed to active infection of the myocardium in the great majority of cases rather than to any mechanical defect Further they conclude that heart failure during the later decades is generally produced by additional causes *such as arterial hypertension or pulmonary hypertension sclerosis* of the coronary vessels or myocardial degeneration Finally it may be mentioned that in 100 autopsied cases of rheumatic heart disease at ages over 20 years *Juca and White* (1944) found histological rheumatic activity in 31 per cent of 16 cases in the third decade in 26 per cent of 27 in the fourth decade in 25 per cent of 15 in the fifth in 17 per cent of 23 in the sixth in 8 per cent of 13 in the seventh and in 1 out of 5 cases in the eighth decade

The finding of 2 (possibly 4) per cent of deaths with clinical signs of rheumatic recurrence in the writer s series is in accord with the findings by *Graham et al* of 1 per cent *of deaths with clinical rheumatic recurrence in 100 autop*sied cases of mitral stenosis (including some with mitral aortic disease)

Subacute bacterial endocarditis was the cause of death in 4 patients (2 per cent) 2 females aged 25 and 26 and 2 males aged 38 and 49 Among the four cases of sepsis previously mentioned there may possibly have been some with subacute bacterial endocarditis but even though these were included the incidence of this complication would not exceed 4 per cent in the present series

Aastrup found 1 death of probable subacute bacterial endocarditis in 50 deaths of mitral stenosis (2 per cent) and *Grant* mentioned 14 deaths of this complication in 100 deaths of mitral stenosis In series of autopsied cases of mitral stenosis and of combined mitral aortic disease *Stone and Feil* found an incidence of subacute bacterial endocarditis of 8 per cent and *Graham et al.* found 11 per cent It was emphasized in both publications that subacute bacterial endocarditis is more frequent in the case of aortic valvular disease than in isolated mitral stenosis Accordingly the incidence of subacute endocarditis higher in most series of rheumatic valvular disease in general *Laws and Levin* found this complication in 43 out of 148 deaths (29 per cent) *Davis and Weiss* (1935) in 47 out of 229 (17 4 per cent) *Grant* in 106 out of 305 (34 per cent) whereas *DeGraff and Lingg* found only 5 6 per cent who died of subacute bacterial endocarditis among 614 deaths of rheumatic heart disease

Death owing to *congestive failure* occurred in 98 cases (52 per cent) This corresponds to *Aastrup* s 56 per cent and *Grant* s 57 per cent among patients with isolated mitral stenosis who died Among patients with rheumatic heart disease *DeGraff and Lingg* found 45 per cent who died of congestive failure

Acute pulmonary oedema was the cause of death in 9 patients (5 per cent) this group will be dealt with in greater detail in the section on pulmonary oedema

Sudden death occurred in 1 case (1 per cent) and according to the literature is a rare phenomenon in mitral stenosis In *Grant* s series 3 out of 100 patients with mitral stenosis died suddenly whereas sudden death in this type of valvular disease was not seen in *Aastrup* s series

When the 7 cases classified as *heart death* owing to insufficient information about the last phase of the disease are included 116 patients in all (61 per cent) died of *heart failure*

Thrombo embolic complications were the cause of death in 41 cases (22 per cent) 19 of these patients died of cerebral emboli (10 per cent) 9 died of other arterial emboli in the systemic circulation (5 per cent) and 14 died of pulmonary emboli (7 per cent) These complications will be mentioned in greater detail in the sections on emboli in the systemic and the pulmonary circulation

Pneumonia was the cause of death in 6 cases (3 per cent)

Causes of death and age at death

TABLE 26
Causes of Death in Relation to Age in Isolated Mitral Stenosis

Cause of death	14-19	20-29	30-39	40-49	50-59	60-69	70-79 y	Total
Congestive failure	1	7	17	25	29	17	3	99
Acute pulmonary oedema	1	2	4	2	–	–	–	9
Sudden death	–	–	1	–	–	–	–	1
Heart death	–	1	–	1	3	2	–	7
Cerebral emboli	–	–	2	6	5	5	1	19
Other arterial emboli	–	–	1	3	1	2	1	8
Pulmonary emboli	–	1	4	6	1	2	–	14
Active rheumatic fever	1	2	–	–	–	–	–	3
Subacute bact endocarditis	–	2	1	1	–	–	–	4
Sepsis	–	–	3	–	1	–	–	4
Pneumonia	–	2	1	2	1	–	–	6
Other causes of death	–	–	3	6	4	2	–	15
Total	3	17	37	52	45	30	5	189

Table 26 shows the relation of the causes of death to the age at death It appears that active rheumatic fever affects the quite young and that subacute bacterial endocarditis affects the young patients whereas the cases of pneumonia in the present series are fairly evenly distributed on the various age groups Acute pulmonary oedema as cause of death chiefly occurred in the young patients whereas congestive failure comprised all age groups though the incidence is somewhat higher in the older age groups Arterial and pulmonary emboli were causes of death chiefly in middle aged and elderly patients Finally the group Other causes of death chiefly involved the middle age groups

These findings are in accord with *Aastrup*s and with *Laws and Levine*s experiences

Autopsy findings

Autopsy was performed in 85 cases of the present series only cases autopsied by experienced pathologists have been included

The distribution of the series according to age and special findings is given in Table 27

TABLE 27

85 Autopsied Cases of Mitral Stenosis Arranged According to Age and Special Complications (Degree of Stenosis Calcification of Mitral Valve other Valvular Changes Adherent Pericardium and Coronary Sclerosis)

Total	14–19 1	20–29 6	30–39 17	40–49 25	50–59 22	60–69 11	70–79 y 3	Total 85
Severe stenosis	1	3	16	22	15	6	–	63
Slighter stenosis	–	3	1	3	7	5	3	22
Calcification of mitral valves	–	–	4	11	7	4	1	27
Aortic valvular disease	–	–	–	–	–	–	–	
Sequelae of aorta endo carditis	–	1	2	1	4	4	1	13
Tricuspid valve stenosis	–	2	–	1	–	2	–	5
Adherent pericardium	–	1	–	2	1	2	–	6
Acute pericarditis	1	1	–	–	2	–	–	4
Atheromatosis of coronary arteries	–	–	3	8	5	5	1	22
Arteriosclerosis of coro nary arteries		–	–	5	3	1	2	11

The available descriptions of the mitral ostium generally only mention whether a stenosis was present In many cases therefore the degree of any mitral incompetence in the presence of stenosis was not stated

Isolated mitral incompetence

In a follow up of all cases classified as rheumatic valvular disease only one case of isolated mitral incompetence verified at autopsy was found It was that of a woman who had not been suffering from any known rheumatic infection after 4 years cardiac complaints she died in complete congestive failure at the age of 56

The writer s series of autopsied cases collected on the basis of the clinical diagnosis of rheumatic valvular disease thus contains only 1 case of mitral incompetence and 85 cases of mitral stenosis

Other series of autopsied cases generally show a somewhat higher incidence of pure mitral incompetence *Aastrup s* series had 4 cases of mitral incompetence in 27 cases of isolated mitral disease (15 per cent) *Henschen* (1916) found 24 cases of mitral incompetence in 128 of mitral disease (19 per cent)

Aas (1948) had 28 cases in 146 of mitral disease (20 per cent) and *Cabot* had 7 cases of mitral incompetence in 114 of mitral disease (6 per cent) *Chapelle et al* (1934) mentioned 5 cases of mitral incompetence among 103 of mitral disease including a number of patients with other complicating valvular disease

It has been maintained by *Cabot Mackenzie Lewis* and others that pure mitral incompetence is seldom the actual cause of death When patients with pure mitral incompetence die it is generally from complications This view is confirmed by the series published by *Cabot* and by *Aastrup* as all diagnosed cases of mitral incompetence had complications which were accepted as cause of death In *Henschen*s series mitral incompetence was the actual cause of death in only 2 out of 24 cases and both were elderly patients In contrast with this view it was asserted by *Dana and Reidy* (1936) that the pure mitral incompetence is not infrequently the actual cause of death The authors themselves found 6 patients with pure mitral incompetence without complications who died before the age of 50 in a series of 150 cases of mitral disease including 74 with mitral stenosis Similar viewpoints were maintained by *Movitt and Gerstl* (1953) who mentioned 4 patients with pure mitral incompetence who died in congestive failure at ages between 42 and 56 years All things considered it must be concluded that the literature contains no publications which can convincingly shake the view that pure mitral incompetence is seldom the actual cause of death in patients under 50 years of age

Degree of the mitral stenosis

With regard to the degree of the mitral stenosis the present series has been divided according to the available descriptions into severe and slight stenoses All cases in which the ostium was narrower than or passable only with difficulty by one finger were classified as severe stenoses whereas all cases in which the ostium could be easily passed by one finger but only with difficulty by two were classified as slight stenoses This classification should of course be considered with some reservation as the series was not examined especially with a view to this However the general distribution of the series according to age and the degree of stenosis given in Table 27 shows that there is an increasing frequency of slight stenosis with advancing age at death so that most patients with slight stenosis live longer than those with severe stenosis this was also to be expected In contrast with these findings *Chapelle et al* and *Graham et al* found no distinct relation between the degree of the stenosis and the age at death

Calcifications in the mitral valves have been described in 27 patients (32 per cent) 4 were between 30 and 39 years 11 between 40 and 49 7 between 50 and 59 4 between 60 and 69 and 1 patient was 8 years It may be mentioned

that the average survival time after the first rheumatic infection was 36 yea (varying from 19 to 50 years) and that the average survival time after the onset of the heart symptoms was 15 years (varying from 1 to 44 years)

Affection of the aortic valves is in advance excluded from the series b sequelae of previous endocarditis on the aortic valves were noticed in 13 cas

Tricuspid valve affection – Tricuspid stenosis was found in 5 patients women at ages of 23 26 46 63 and 66 years The average age was 44 8 yea thus not differing much from the average age of 47 0 in the total series T incidence of tricuspid valvular affection in mitral stenosis without aortic val vular disease in the present series (6 per cent) is in fairly good conformity with the statements in similar series in the literature *Aastrup* found 2 cases with tricuspid valvular disease in 23 of mitral stenosis (9 per cent) *Stone and Fei* had 5 cases in 59 of mitral stenosis (9 per cent) and *Graham et al* had 4 in 54 (7 per cent) The incidence of tricuspid valvular affection in mitral steno s without aortic valvular disease may thus be expected to be from 6 to 9 per cent Tricuspid incompetence owing to endocarditis has not been described with certainty in the present series but in 2 cases the description of the autopsy ventilated the diagnosis of functional tricuspid incompetence

Adherent pericardium was found in 6 out of 85 patients (7 per cent) The incidence is somewhat lower than that given in *Aastrup* s series (30 per cent) but rather corresponds to the findings in the series of *Stone and Feil* (10 pe cent) and *Graham et al* (11 per cent)

The *weight of the heart* was given in 61 cases In 10 it was between 300 an 399 gm in 17 between 400 and 499 gm in 20 between 500 and 599 gm in between 600 and 699 gm in 2 between 700 and 799 gm and in 3 cases it wa between 800 and 899 gm

Changes in the coronary arteries – Atheromatosis of the coronary arterie was found in 22 patients 19 of whom were over 40 years Arteriosclerosis of the coronary arteries was ascertained in 11 patients all over 40 years In 1 of these cases a woman aged 47 autopsy revealed a fresh anterior wall infarction

Changes in the coronary arteries thus occurred in 33 patients in all (39 per cent) and in 30 out of 61 patients over 40 years (49 per cent) Arteriosclerosis alone was found in 11 out of 61 patients over 40 years (18 per cent)

These incidences of pathologic anatomical signs of coronary affection are in accord with *Chasnoff and Silver* s experiences (1951) In 66 cases of rheumatic heart disease over 40 years of age these authors found atherosclerosis of the coronary vessels in 40 per cent and considerable constriction of these in 91 per cent *Wartman and Hellerstein* (1948) found coronary sclerosis or thrombosis in 16 out of 49 autopsied cases of rheumatic heart disease over 45 years

(30 per cent) this incidence corresponded to that of coronary sclerosis in the whole of their autopsied series over 45 years (25 per cent) Other authors find that coronary sclerosis is somewhat rarer in rheumatic heart disease *Gardner and White* (1949) thus found pathologic anatomical coronary disease in only 32 out of 436 autopsied cases of rheumatic heart disease (7 per cent) In *Aastrup* s series slight atheromatous changes in the coronary arteries were mentioned in 5 out of 23 cases of isolated mitral stenosis (22 per cent) whereas severe coronary sclerotic changes were not observed

Angina pectoris was present in 5 cases in all in the writer s series of autopsied cases Changes in the coronary arteries were found in 3 atheromatosis in 1 and arteriosclerotic changes in 2 In the last two patients the coronary arteries were normal

These findings are in accord with *Chasnoff and Silver* s series in which only 10 out of 90 cases with angina pectoris showed coronary sclerotic changes

Angina pectoris in mitral stenosis without coronary sclerosis demonstrable post mortem has also been described by other authors The literature on this subject has been reviewed by *Blackford* (1940) who reported 2 cases of this nature himself

The pathogenesis of this pain is supposed to be that the systemic output in severe mitral stenosis cannot fulfil the requirements of the coronary circulation on exertion in some cases possibly because the enlarged left atrium compresses or kinks a coronary artery

Renal changes were found in 39 patients in all (46 per cent) Nephrolithiasis was present in 3 patients hydronephrosis in 1 senile atrophy in 1 nephrosclerosis in 4 including 1 with cicatrices after kidney infarction acute pyelonephritis in 1 who also presented cicatrices after kidney infarctions

Signs of kidney infarctions were found in 39 patients in all in 29 as the only change 5 patients had fresh or healed infarctions and 24 cicatrices only after healed infarctions No relation could be found between the arterial blood pressure level and the presence of old standing kidney infarctions The incidence of these and of other kidney disorders is in accord with the findings in *Aastrup* s series

Survey of the Patients Surviving at the Time of Follow up

Eighty two out of the 271 patients with mitral stenosis (30 per cent) were alive at the time of the follow up The period of observation for this group varied from 3 to 20 years averaging 9 7 years

Age and Sex incidence

The group of survivors comprised 62 females and 20 females the age incidence is shown in Table 28

TABLE 28

Age and Sex incidence of Surviving Patients with Mitral Stenosis

	20–29	30–39	40–49	50–59	60–69	70–79	Total
Males	2	4	6	[illegible]	2	0	20
Females	1	2	30	20	8	1	62
Total	3	6	36	26	10	1	82

This series is distributed with 3 patients in the age group 20–29 years 6 in the age group 30–39 36 in the group 40–49 26 in the group 50–59 10 in the group 60–69 years and 1 over 70 years 37 out of 82 patients in all were over 50 years (45 per cent)

The average age for the whole series of survivors is 49 1 years (females 50 and males 46 7 years)

The average age of survivors (49 1 years) was thus higher than that of the dead (47 0 years) in the writer s series

Clinical state at the follow up

Of the 82 survivors 72 were followed up in Medical Department B the University Hospital Copenhagen 6 were examined in their homes and in 4 cases information about the condition at the time of the follow up was available only by letter Mention may first be made of the last group

I *Patients reporting their condition at the time of the follow up by letter only*

(1) *Case 80* – A woman aged 36 at the first examination had had rheumatic fever when she was 25 and 31 and heart symptoms from the 34th year She had sinus rhythm The cardio thoracic index was 50 and there were no signs of right heart failure She had been considered belonging to Class III 16 years later she stated that her condition had remained unchanged

(2) *Case 167* – A man aged 28 at the first examination had had rheumatic fever when he was 14 23 and 27 and heart symptoms from the 14th year He had sinus rhythm The cardio thoracic index was 49 and there were no signs of right heart failure He had been placed in Class II 10 years later he stated that his condition had remained unchanged and that he was working as a gardener in Sweden

(3) *Case 178* – A man aged 19 at the first examination had had rheumatic fever when he was 11 18 and 19 years and heart symptoms from the 17th year He had sinus rhythm The cardio thoracic index was 42 and there was no right heart failure He had been placed in Class II Examination in another hospital 9 years later described the state of the heart as unchanged

(4) *Case 181* – A man aged 58 at the first examination had had no rheumatic infections He had said that he had heart symptoms from the age of 58 He had sinus rhythm at the first examination The cardio thoracic index was 50 and there was no right heart failure He had been placed in Class II Examination in another hospital 9 years later revealed auricular fibrillation and right heart failure his physical activity had been much reduced

In this part of the series 1 out of 4 cases thus definitely suggested progression of the mitral stenosis

II *Series of cases followed up*

Twelve out of the 78 patients followed up by the writer presented definite signs of complicating aortic valvular disease which had not been ascertained at the first examination 66 patients showed signs of mitral stenosis only The cases followed up are dealt with as a whole in the following only the most important findings at the follow up being mentioned especially with a view to an assessment of the progression of the mitral stenosis Special complications during the course of the disease will be mentioned in the separate sections in the following

Heart rhythm

Sinus rhythm was found at the follow up in 24 patients (31 per cent) auricular fibrillation in 54 (69 per cent) Table 29 shows that the incidence of auricular fibrillation is distinctly increasing with advancing age

TABLE 29

Heart Rhythm in Relation to Age in Series of Cases Followed up

	20–29	30–39	40–49	50–59	60–69	70–79 years	Total
Sinus rhythm	1	3	13	6	1	0	24
Auricular fibrillation	1	2	23	19	8	1	54
% with auricular fibrillation	50	40	64	76	89	100	69

Thirty six patients had auricular fibrillation at the first examination Among 42 patients with sinus rhythm at the first examination auricular fibrillation

developed in 18 (or 43 per cent of patients with sinus rhythm) during the period of observation

Right heart failure

Right heart failure was ascertained at the follow up in 32 out of 78 patients (42 per cent)

At the first examination *right heart failure* was found in 9 patients and the syndrome was ascertained again in 8 but had disappeared in 1 of these patients

Right heart failure developed in the course of the period of observation in 24 out of 69 patients (35 per cent) who had no such signs at the first examination

Heart size

Roentgenography was performed in 71 cases at the follow up The distribution *of the series according to cardio thoracic indices is shown in Table 30*

TABLE 30

Cardio thoracic Indices in the Series Followed up

Index	Number of patients	Index	Number of patients	Index	Number of patients
46	1	58	2	68	1
48	1	59	3	71	1
49	1	60	2	72	1
51	4	61	3	73	1
52	3	62	1	75	2
53	4	63	3	79	1
54	9	64	4	81	1
55	4	65	3	86	1
56	3	66	3	87	1
57	5	67	2		

In 3 patients the cardio thoracic index was under 50 in 37 between 51 and 59 in 22 between 60 and 69 and in 9 patients it was higher than 70

A rise in the numerical value of the cardio thoracic index of 10 per cent or more was ascertained in 40 out of 71 patients (56 per cent) whereas the differences in the index value were less than 10 per cent in 31 cases (44 per cent)

Physical activity

Table 31 shows that 16 patients belonged to Class II at the follow up 44 to Class III and 18 to Class IV

TABLE 31

Degree of Physical Activity in Relation to Age at the Time of Follow up

	°0–°9	30–39	40–49	50–59	60–69	70- 9 y	T ı l
Class II	0	2	7	6	1	0	16
Class III	1	2	°0	14	6	1	44
Class IV	1	1	9	5	2	0	18
Total	2	5	36	°₅	9	1	78

Among these 78 cases the classification was unchanged in 44 (56 per cent) 16 belonging to Class II and 28 to Class III

In 34 cases the patients were classified in a poorer class than at the first examination (44 per cent) 19 patients originally belonged to Class II 16 were placed in Class III at the follow up and 3 were transferred to Class IV 15 patients originally belonging to Class III were placed in Class IV at the follow up

Total estimate of all cases followed up

Judging by the separate findings mentioned above – auricular fibrillation right heart failure heart size and degree of physical activity – a considerable number of cases showed distinct signs of progression of the heart disease Not considering the heart size as this was assessed only in some of the cases followed up a total survey of the number of patients showing signs of progression of the heart disease at the follow up may be given here The progression is thus judged by the occurrence of auricular fibrillation the presence of right heart failure or by distinct deterioration of the physical activity

Among patients who at the first examination were in Class II and had sinus rhythm (and no signs of right heart failure) i e the mildest case of the original series the condition according to the criteria mentioned had remained unchanged at the follow up in 10 out of 27 patients (37 per cent) and had aggravated in 17 (63 per cent) In 5 out of these 17 patients (19 per cent) the physical activity had deteriorated 6 (22 per cent) had developed auricular fibrillation (in 2 with simultaneous deterioration of the physical activity) and 6 (22 per cent) had developed right heart failure auricular fibrillation and deterioration of the physical activity The average period of observation of this group was 13 4 years

Among patients who at the first examination belonged to Class III and had sinus rhythm (without signs of right heart failure) the condition at the follow up was unchanged in 5 out of 14 (36 per cent) and had aggravated in 9 (64

per cent) 3 of the latter had developed right heart failure but still had sinus rhythm 3 had developed auricular fibrillation without right heart failure and 3 showed auricular fibrillation right heart failure and a distinct deterioration of the physical activity The period of observation of this group averaged 8.7 years

Among 37 patients who had auricular fibrillation or right heart failure or both at the first examination the findings were as follows —

In 10 patients with auricular fibrillation and no signs of right heart failure belonging to Class II the condition had remained unchanged in 2 (20 per cent) and had aggravated in 8 (80 per cent) In 5 patients deterioration of the physical activity was the only sign of aggravation in 3 right heart failure had developed simultaneously with a reduction of the physical activity The average period of observation of this group was 8 0 years

Among 18 patients with auricular fibrillation and no signs of right heart failure belonging to Class III the condition had remained unchanged in 9 (50 per cent) and had aggravated in 9 (50 per cent) with development of right heart failure and deterioration of the physical activity The period of observation of this group averaged 8 1 years

In a group of 9 patients with right heart failure all belonging to Class III (8 with auricular fibrillation as well) the condition had improved in 1 case with abatement of right heart failure remained unchanged in 3 cases and had aggravated in 5 with reduction of physical activity The period of observation of this group averaged 7 0 years

Summing up it can be said that the follow up of the surviving patients from the criteria mentioned showed that the heart disease had aggravated during the period of observation in quite a considerable number of cases In the best group (patients in Class II with sinus rhythm and without signs of right heart failure) the condition had remained unchanged in only 37 per cent whereas it had aggravated in 63 per cent In the other groups the condition had gradually aggravated correspondingly

The fact that 4 patients were not followed up cannot alter this conclusion

RHEUMATIC INFECTION AND THE COURSE OF MITRAL STENOSIS

Incidence of rheumatic infection

In the writer s series of cases of clinically isolated mitral stenosis information about rheumatic infection was available in 159 out of 271 patients (58 per cent) 36 out of 70 patients observed after the 50th year of life had had rheumatic infection (52 per cent)

The infection was in the form of acute rheumatic fever in 132 cases acute rheumatic fever and chorea minor in 10 scarlatinal rheumatoid arthritis in 3 and chorea minor without rheumatoid arthritis in 14 cases

The incidence of rheumatic infection in the present series of mitral stenosis is in accord with the experiences reported in the literature In clinical series of mitral stenosis the incidence of a past history of rheumatic infection is thus in *Denmark* 69 per cent (*Aastrup* 1937) in *Norway* 49 per cent (*Jervell and Brytting* 1938) in *Sweden* 55 per cent (*Nylin* 1952) in the *U S A* 53 per cent (*Levine and Fulton* 1928) In a clinical series of rheumatic heart disease *DeGraff and Lingg* (1935a) had no information about rheumatic infection in about 30 per cent of the cases and it is in accord with the experiences mentioned that *Warburg* (1931) stated that information about rheumatic infection was lacking in from 25 to 50 per cent of cases with rheumatic valvular disease

In autopsied series of mitral stenosis the following incidence of rheumatic infection is given *Cabot* (1914) 62 per cent and *Stone and Feil* (1934) 64 per cent In autopsied series of rheumatic valvular disease *Laws and Levine* (1933) found 66 per cent with rheumatic infection *Davis and Weiss* (1935) had 77 per cent whereas *Friedberg and Tartakower* (1931) found 16 per cent in their series of hospitalized cases but only 29 per cent in their series of much older cases from the nursing home

Age at first rheumatic infection

The age at the first rheumatic attack is known in 157 cases The earliest attack set on at the age of 4 years the latest at the age of 45 The age and sex incidence at the first rheumatic attack is shown in Fig 7 It appears that the first infection is most frequent in the age group 10–14 years then follow the age groups 0–9 years and 15–19 years whereas there are comparatively few cases at ages over 20

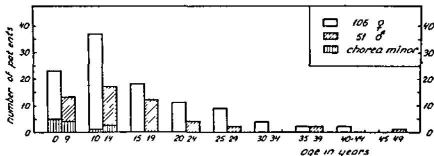


Fig 7

Age at first rheumatic infection in 157 cases of isolated mitral stenosis

The average age at the first rheumatic infection was 15 4 years for the whole group 16 0 years for all with acute rheumatoid arthritis and 8 3 years for the group with chorea minor only

Correspondingly *Coombs* (1924) found an average age of 14 4 years for mitral disease at the first rheumatic infection For rheumatic valvular disease *Aastrup* gave the average age of 17 years at the first infection in all patients, 17 years in the case of acute rheumatoid arthritis and 11 years in chorea minor *DeGraff and Lingg also found an average age of 17 years in rheumatic* heart disease

The relative age incidence at the first rheumatic infection in the present series of cases is given in Table 32 which shows that 92 per cent had their first rheumatic infection before the 30th year Correspondingly *Aastrup* fou d an incidence of initial rheumatic infection before the 30th year of 92 per cent in cases of rheumatic valvular disease and *DeGraff and Lingg* found 89 per cent in rheumatic heart disease

In clinical series of rheumatic heart disease *Simmonds* (1934) found 94 per cent and *Willius* (1927) 85 per cent In autopsied series of rheumatic valvular disease *Davis and Weiss* (1934) had 82 per cent and *Friedberg and Tartakower* (1931) 88 per cent

In accord with series of rheumatic valvular disease reported in the literature the present series thus shows a very high incidence of initial rheumatic infection before the 30th year

TABLE 3

The Relative Age I cidence at the First Rheumatic Infection

	P t r I l t d m t al ste ; 157 pat t	Se of he m t c fe p t d ı th l te at e		
		A t al 1951 194 pat e t	Eble t e 194 210 pat t	Fd t m) 1935 850 p t n
0– 9 years	23	20	20	8
10–14	34	12	27	15
15–19	19	18	15	2[illegible]
20–24	9	1[illegible]	12	16
25–29	7 9[illegible]	9 74	11 8[illegible]	10 74
30–34	3	9	5	8
35–39	3	[illegible]	6	5
40–44	1	6	1	4
45–49	1	2	2	[illegible]
50–54	–	2	–	[illegible]
55–59	–	[illegible]	1	2
60 and more	–	–	–	3

*) Edstrom s series was divided into age groups 0–10 11–15 etc

Table 32 gives the relative age incidence in 3 Scandinavian series of rheumatic fever In *Arnso Hastrup and Brochner Mortensen* s Copenhagen series of 1926–40 the incidence of initial infection before the 30th year was 74 per cent whereas *Ehlertsen* (1942) in a series from Aarhus of the years 1921–30 found an incidence of 85 per cent In a Swedish series of 1911–33 *Edstrom* (1935) found an incidence of 74 per cent of initial infections before the 30th year These three Scandinavian series of initial rheumatic infection thus show an age incidence differing with the same tendency from that found in the present series the comparison confirms the generally accepted view that valvular disease is most frequent in patients with an early rheumatic infection

Sex incidence

In the present series details of rheumatic infection were available in 51 out of 77 males (66 per cent) and in 106 out of 194 females (53 per cent) Fig 7 shows that most of the males had had their first rheumatic infection at an earlier age than the females The average age at the first attack was 14 0 years in males and 16 3 years in females

Among males 82 per cent had their first infection before the 20th year and 94 per cent before the 30th year the corresponding figures in females were 72 per cent and 92 per cent

This unequal sex incidence according to age at the initial rheumatic infection is in close conformity with the findings in *Ehlertsen* s Danish and *Wilson* s North American series of rheumatic fever *Edstrom* on the other hand found no definite difference between the sexes in this respect and in *DeGraff and Lingg* s large series of rheumatic heart disease there was no definite difference between the sexes with regard to age at the first rheumatic infection

With regard to the numerical distribution of males and females in the present series 33 per cent of males and 67 per cent of females this is close to *Jervell and Gryttings* 36 per cent of males and 64 per cent of females These findings however differ from the sex incidence in ordinary series of rheumatic fever in which the males generally represent from 40 to 50 per cent of the whole series (*Ehlertsen* 41 per cent *Wilson* 45 per cent *Edstrom* 48 per cent and *Mackie* 50 per cent) This is in accord with the classic experience that it is women who chiefly develop mitral stenosis

Rheumatic recurrence

Rheumatic recurrence was seen in 86 out of 157 patients (55 per cent) namely in 28 out of 51 males (55 per cent) and in 58 out of 106 females (55 per cent)

The relationship between recurrences and age at the initial rheumatic infection is shown in Table 33 In the groups who had the first infection before

TABLE 33
Number of Rheumatic Recurrences in Relation to Age at First Attack

Age groups	Total	No recurrence	With recurrence	1 recurrence	2 recurrences	3 recurrences or more	Recurrence
4– 9 years	36	12	24	4	10	10	67
10–14	54	20	34	14	9	11	63
15–19	30	14	16	6	8	2	53
20–24	15		8	6	2	–	53
25–29	11	8	3	2	1	–	2
30–34	4	3	1	1	–	–	25
35–39	4	4	–	–	–	–	
40–44	2	2	–	–	–	–	–
45–49	1	1	–	–	–	–	–
Total	157	71	86	33	30	23	55
%	100	45	55	22	19	14	–

the 15th year about 65 per cent of the patients had rheumatic recurrence Patients who had their first infection between the 15th and 24th years had recurrences in 53 per cent of cases and those who had their first infection between the 25th and 34 years had an average of 26 per cent of recurrences Patients in whom the first rheumatic infection occurred later showed no recurrences in the present series

The number of recurrences is distributed thus 22 per cent of the total series with rheumatic infection had 1 recurrence 19 per cent had 2 recurrences and 14 per cent 3 or more recurrences As will appear from Table 33 it was primarily patients with early rheumatic infection who had repeated recurrences

Compared with other series of mitral stenosis reported in the literature the present one has a high incidence of rheumatic recurrences In *Grant's* series there were thus only 36 per cent of rheumatic recurrences *Stone and Feil's* series of autopsied cases of mitral stenosis showed 33 per cent of rheumatic recurrences and *Friedberg and Tartakower's* series of autopsied cases of rheumatic valvular disease had 31 per cent of recurrences

The finding of 53 per cent of rheumatic recurrences in the present series is much more in accord with *Thlertsen's* Danish series of rheumatic fever which showed 50 per cent of recurrences after 10 years and with the similar series published by *[illegible]om* from Sweden which had 50 per cent of recur[illegible] the pr[illegible] more than 1 recurrence was found in 33 per cent

of the patients in those published by *Ehlertsen* and *Edstrom* in 24 and 22 per cent respectively, i.e. there was a higher incidence of repeated recurrence in the present series. It should however be noted that the latter covers a longer period of observation than the former two series.

The tendency to decreasing frequency of recurrence with advancing age at the initial rheumatic infection in the present series is in close conformity with *Ehlertsen's* and *Edstrom's* experiences.

Interval

With regard to the intervals between the initial infection and the first recurrence the present series is also in accord with that of *Ehlertsen* as they both show about 20 per cent of recurrences after more than 10 years. *Edstrom* found only 6 per cent, but here too differences in the period of observation may play a part.

The interval between the initial rheumatic infection and the first recurrence in the present series differed from less than 1 year to 36 years. The intervals are unknown in the case of 4 patients, but are otherwise distributed as shown in Table 34.

TABLE 34
Interval between Initial Rheumatic Infection and First Recurrence

Age group at initial infection	Interval						
	0–4	5–9	10–14	15–19	20–24	25–29	30 years and more
4– 9 years	12	7	2	–	–	–	–
10–14	13	9	4	4	1	1	1
15–19	11	1	2	–	–	–	2
20–24	4	3	–	–	–	–	1
25–29	–	3	–	–	–	–	–
30 years and more	1	–	–	–	–	–	–
Total	41	23	8	4	1	1	4
%	78		22				

The recurrences in the present series appeared most frequently during the first ten years after the initial infection in a total of 78 per cent of the cases. The last 22 per cent appeared at intervals of from 10 up to 36 years.

Of the total series of 157 patients about whom the time of the first rheuma tic infection is known 111 died and 46 survived at the time of the follow up

The average survival time after the first rheumatic infection for all dead patients was 30 1 years for 42 dead males 31 0 years and for 69 dead females 29 5 years

The average survival time after the first rheumatic infection for the 46 survivors was 33 3 years for 9 males 32 1 years and for 37 females 33 7 years

The average survival time was thus higher for survivors than for the dead

The survival time varied from 5 to 56 years

The median survival time of the whole group was 35 0 years

Duration of life

The average age of the dead patients with rheumatic infection was 45 years for the whole series 45 1 years for males and 46 2 years for females

The average age of the survivors was 48 8 years for the whole series 46 years for males and 49 3 years for females

Age at initial rheumatic infection duration of life and survival time

In order to illustrate the significance of age at the initial rheumatic in fection to the survival time the survival curves from the time of the initi infection have been calculated with the technique mentioned on page 45 f the following three groups (1) 36 patients who had their initial infection ages from 0 to 9 years (2) 84 patients whose initial infection occurred at ag from 10 to 19 years and (3) 37 patients who had their initial infection a ages over 19 years

The survival curves in Fig 8 show that the group with initial infection a ages from 0 to 9 years had 75 per cent of survivors after 25 years 50 per cent after 38 years and 25 per cent after about 50 years from the time of the initial infection The survival curve is of almost the same appearance in the group of patients who had their first infection at ages from 10 to 19 years as 75 per cent survived 25 years 50 per cent 36 years and 25 per cent 46 years The group of patients who had their first infection after the 20th year shows 75 per cent surviving after 21 years 50 per cent after 27 years and 25 per cent after 37 years i e somewhat shorter survival times than those of the two preceding groups

With regard to the duration of life an analysis of the series showed that the group with the initial infection at ages from 0 to 9 years had 75 per cent surviving at the 33rd year of life 50 per cent at the 44th 25 per cent at th 56th and 16 per cent at the 65th year of life The group with the first in

fection at ages from 10 to 19 years had 74 per cent surviving at the 39th year of life 50 per cent at the 49th 25 per cent at the 61st and 16 per cent. at the 65th year of life The group of patients who had their first infection after the 19th year showed 75 per cent surviving at the 51st year of life 50 per cent at the 58th and 25 per cent at the 62nd year of life

It thus appears that patients in the present series who had a first rheumatic infection of early onset had a shorter duration of life than those who had their first infection later

Rheumatic recurrence and survival time

In order to assess whether rheumatic recurrences influenced the survival time after the rheumatic infection the survival was calculated for patients with initial rheumatic infection before the 20th year after the series had been divided into the following 3 groups (1) 46 patients with one rheumatic attack (average age 13 1 years) (2) 24 patients with one rheumatic recurrence (average age 12 3 years) and (3) 50 patients with two or more rheumatic recurrences (average age 12 0 years)

The survival curves for these three groups are given in Fig 9 which shows that the group with two or more recurrences does not differ decisively from the two other groups with regard to survival Thus in the present series

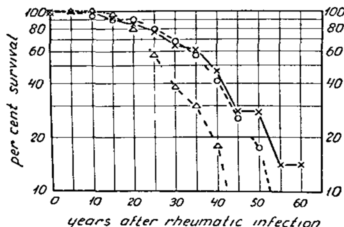


Fig 8

The curve shows the survival time (plotted along the abscissa) in relation to the age at the first rheumatic infection The series is divided into 3 groups Initial infection before the 10th year X———X between the 10th and 19th years O----O after the 20th year △---△

The ordinate shows the survival percentage of the original series

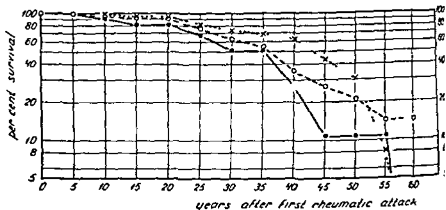


Fig 9

Survival after the initial rheumatic infection in 3 groups of the same age under years Patients with one rheumatic attack O------O with 2 attacks ●—— and with 3 attacks X X

nothing suggested that the number of clinical rheumatic recurrences definit influenced the survival time after the first rheumatic infection

Discussion

The survival times reckoned from the first rheumatic infection were markably long in the present series But it should be borne in mind that original series had a high average age and included comparatively few yo patients and no children A number of the severest cases of rheumatic mi stenosis can thus be excluded in advance from the series The comparati long period of observation must also be considered since as previously m tioned this will tend to give long survival times

In the present series the survival times after the first rheumatic infect are higher than those given in most series of rheumatic heart disease repor in the literature Among 50 patients with mitral stenosis who died *Aasli* found an average survival time of 23 years Among cases of rheumatic he disease observed till death occurred *Cabot* (1914) found a survival time about 20 years *Willius* (1927) 21 years and *Friedberg and Tartakower* (19 found 20 years in the case of males and 25 years in females in the hospi series and 38 years in patients in the nursing home Finally it may be me tioned that *Coombs* (1924) calculated a survival time of about 30 years aft the rheumatic infection

AGE AT ONSET OI HEART SYMPTOMS AND COURSE OI MITRAL STENOSIS

In a small number of cases the heart symptoms in mitral stenosis set on immediately after the first rheumatic infection but otherwise the rule is that there is a symptomless period between the initial rheumatic infection and the occurrence of heart complaints In cases without a past history of rheumatic infection the onset of the first heart symptom will generally be the earliest date in the course of the disease

As the occurrence of heart symptoms in mitral stenosis generally indicate that the heart can only with difficulty fulfil the normal demands the patient s age at the first signs of heart trouble will be a usable starting point in the study of the course of the disease The value hereof is impaired to some degree by the fact that the heart symptoms in mitral stenosis rather often develop gradually It may thus be difficult for the patient to state the exact date of onset and nervous heart symptoms may distort the picture in some cases In spite of this uncertainty the patient s age at the onset of the first heart symptom is nevertheless a valuable date in the description of the course of the disease and in the estimate of the prognosis an analysis of the age at the onset therefore seems justifiable

In the present series the age at the onset of the first heart symptom is known in 98 per cent of the patients

Age at onset of heart symptoms in the present series

The first heart symptom in the present series of cases of mitral stenosis set on at the age of 5 years at the earliest and at the age of 66 at the latest The average age at the onset of the first symptom was 31 2 years in the 267 cases In females alone the average age was 30 5 in males 33 2 years

TABLE 35

Age at Onset of Heart Symptoms in 967 Case of Mitral Stenosis

	0–9	10–19	0 9	30–39	40–49	50–59	60–6[illegible] y
Number of patients	12	48	67	70	43	28	4
Cumulative percentage	4	3	46	[illegible]1	88	98	100

The distribution of the total series according to age at the onset of the first heart symptom is given in Table 35 which shows the highest incidence in

the age groups from 20 to 39 years The figures of the cumulative distributio show that 4 per cent had developed the first heart symptom before the 10th year 23 per cent before the 20th year 46 per cent before the 30th year 71 per cent before the 40th year 88 per cent before the 50th year and 98 per cent before the 60th year

Patients with a past clinical rheumatic infection develop their heart symp toms at a somewhat earlier age than do patients without clinical rheuma attacks The average age at the onset of the first symptom was 30 0 years in the former group and 33 8 years in the latter

In the case of patients with a past rheumatic infection the interval betwee the first rheumatic infection and the first heart symptom averaged 14 3 yea in females alone 12 3 years in males 18 2 years The dependence of this inte val on the patient s age at the first rheumatic infection appears from Table 3 which shows decreasing intervals with advancing age at the first rheuma infection

TABLE 36

Interval between the First Rheumatic Infection and the First Heart Symptom

	Ag g p t th f t h m t f t n					
	5–9	10–14	15–19	0 4	2–29	o r 30 y
Average interval	17 5	14 3	16 5	14 3	7 4	4 7 yea
Range in years	0–50	0–40	0–36	0–41	0–20	0–20

The most remarkable in the present series of cases is the relatively gi number of patients who develop their first symptoms at an advanced age per cent had their first symptoms after the 40th year and 12 per cent a the 50th year Correspondingly the average age at the appearance of the fi symptom was rather high 31 2 years The series resembling the present most in this respect is *Aastrup s* Danish series of cases of mitral stenosis he the average age of 42 patients was 32 years when the first symptom appear On the other hand the average age at the onset of the first symptom in t present series is higher than that given in *Grant s* series of men in the arm forces where the corresponding figure was 28 2 years and also higher th that given in *DeGraff and Lingg s* cases of mitral stenosis in which the ave age age was 28 years at the onset of the first symptom

The finding of a lower average age at the first symptom in patients wit rheumatic infection than in patients without is confirmed by *Grant s* ser e this is shown in Table 37 which has been calculated from *Grant s* tables

TABLE 37

Average Age at Onset of First Heart Symptom

	Pat t w th h m t f ct	P t ts w th t h m t f t
Present series	30 0 years	33 8 years
Grant s series	26 7	29 ?

The interval between the first rheumatic infection and the onset of the first heart symptom was 14 3 years in the present series Calculation from *Grant s* series shows an interval of 10 years in patients with mitral stenosis who died

These comparisons again characterize the present series as one containing a comparatively great number of cases of mitral stenosis with symptoms setting on late

Survival Time in Relation to the First Heart Symptom

The survival time from the appearance of the first heart symptom varies in the present series from less than 1 year to 52 years The average survival time for 185 dead patients was 14 3 years and for 82 patients who were alive it was 20 5 years

In the case of females the survival time for 131 dead patients averaged 16 1 years and for 62 who were alive it averaged 20 6 years In males the survival time for 54 dead patients averaged 10 1 years and for 20 who were alive 20 3 years

The median survival time of the whole group was 17 8 years

Age at onset of the first heart symptom and survival time

The dependence of the survival time on age at the onset of the first heart symptom appears from Fig 10 which shows the survival curve reckoned from the onset of the symptoms in 5 age groups (1) 60 patients who had their first symptom before the 20th year (average age 13 4 years) (2) 62 patients who had their first symptom between the 20th and the 29th years (3) 70 patients whose first symptom appeared between the 30th and 39th years (4) 43 patients who had their first symptom between the 40th and 49th years and (5) 39 patients whose first symptom appeared after the 50th year

In the group with symptoms before the 20th year 97 per cent survived 5 years 50 per cent 35 years and 23 per cent 50 years In the groups with the first symptom at ages from 20 to 29 and from 30 to 39 years 91 per cent sur

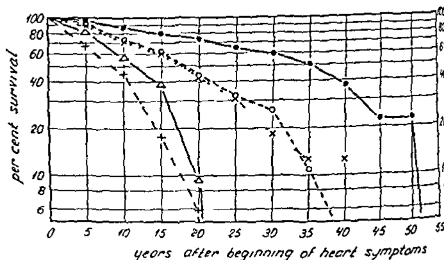


Fig 10

Survival after onset of heart symptoms The series is divided into 5 groups accordi[ng] to age at the onset of the symptoms Before the 20th year ●——● 20–29 yrs ○----○ 30 39 years X----X 40–49 years △——△ and after the 50th year +---+

vived 5 years 50 per cent between 15 and 20 years and about 12 per cent 35 years In the group with the first symptom at ages from 40 to 49 years 8 per cent survived 5 years 50 per cent between 10 and 15 years and no patients of this group survived more than 25 years In the group with the first symptom after the 50th year 69 per cent survived 5 years 50 per cent betwee[n] 5 and 10 years and none survived 25 years

As was to be expected the survival curve shows a distinct tendency to more abrupt fall with advancing age at the onset of the first heart sympto[m]

It may be pointed out that the survival curve shows a fall during the first five years after the onset of the symptoms in all age groups increasing from 3 per cent in the youngest group to 31 per cent in the oldest *Consequently the series has contained quite a large group of patients who died after a very short period with symptoms* namely a total of 31 out of 189 dead patients (16 per cent of all the dead patients) 14 of these developed their symptom before the 40th year 7 between 40 and 49 and 10 after the 50th year

The curves also show the very considerable variation in survival times after the first heart symptom It was most pronounced in the group with heart symptoms before the 20th year It may be pointed out especially that 37 5 per cent of this group survived 40 years after the first symptom and thus attained a duration of life of over 50 years and that a small proportion of the patients had an even longer duration of life With advancing age at the onset of the first symptom the variation of the survival times decreases but an increasing

proportion of the patients will live to be over 50 years of age and the duration of life will be constantly increasing with advancing age at the onset of the first heart symptoms

The question of survival times after the first symptom has not been dealt with very often in the literature Among 50 patients with mitral stenosis who died *Aastrup* found an average survival time of 11 years and *DeGraff and Lingg* found a survival time of 5 years among their patients with mitral stenosis who died

AURICULAR FIBRILLATION IN THE COURSE OF ISOLATED MITRAL STENOSIS

The occurrence of auricular fibrillation is such an important clinical finding in mitral stenosis that a detailed study of the time of onset of this sign during the course of the disease in the present series seems appropriate

Auricular fibrillation auricular flutter and fibrillo flutter will be considered together as these types of arrhythmia alternated rather often in the course of the disease in the same patient The few cases of paroxysmal fibrillation are mentioned separately below In the following analysis these patients have been included from the time when the auricular fibrillation became chronic

The criterion for the presence of auricular fibrillation was electrocardiographic verification of the sign this was achieved in 98 per cent of the cases included in the following analysis In the rest of the cases the presence of the sign was based upon the findings at clinical examination by a specialist in internal medicine In the following the time of onset of auricular fibrillation means the first unquestionable demonstration of the sign according to the criteria mentioned

With this procedure the dating of the onset of auricular fibrillation will often be later than the actual date and the survival times after the onset of auricular fibrillation will be too short on the other hand these figures will be safe minimum figures

Incidence of auricular fibrillation in the present series

The incidence of auricular fibrillation in the whole series is given in Table 38 In 9 out of 189 patients with mitral stenosis who died details of the rhythm are insufficient in the last part of the course of the disease 151 out of the 180 dead patients with known heart rhythm during the last stage of the disease died with auricular fibrillation (84 per cent) Of the survivors 55 out of 79 with known heart rhythm had auricular fibrillation (70 per cent) It thus ap

pears that the great majority of patients with isolated mitral stenosis develop auricular fibrillation during the course of the disease That this development is practically equally frequent in males and females appears from Table 38

TABLE 38
Incidence of Auricular Fibrillation in the Course of Isolated Mitral Stenosis

	Deaths			Survivors		
	Females	Males	Total	Females	Males	Total
Auricular fibrillation	107	44	151	41	14	55
Sinus rhythm	21	8	29	20	4	24
No details available	6	3	9	1	2	3
Total	134	55	189	62	0	89
Auricular fibrillation (% of cases with known rhythm)	83	85	84	67	78	70

Age when auricular fibrillation was ascertained

The relation between age and the demonstration of auricular fibrillation shown in Table 39

TABLE 39
Age when Auricular Fibrillation was ascertained

Age	Females N	Males N	Total N	Cumulative percentage with auricular fibrillation
15–19 years	1	1	2	1
20–24	7	3	10	6
25–29	6	6	12	12
30–34	11	4	15	19
35–39	24	11	35	36
40–44	29	6	35	53
45–49	24	9	33	69
50–54	15	8	23	80
55–59	23	7	30	95
60–64	6	1	7	98
65–69	2	1	3	99
70–74	0	1	1	100
Total	148	58	206	

In 1 per cent of the patients with auricular fibrillation this was first ascer ined before the 20th year in 12 per cent before the 30th year in 36 per cent efore the 40th year in 69 per cent before the 50th year in 95 per cent be re the 60th year and in 99 per cent before the 70th year

The average age when auricular fibrillation was ascertained was 43 8 years the whole series for females 43 9 years and for males 43 4 years

Auricular fibrillation was generally ascertained somewhat earlier among e patients with known rheumatic infection (average age 42 4 years) than nong those without (average age 45 7 years)

It is well established in the literature that auricular fibrillation in mitral enosis increases in frequency with advancing age and that the great majority patients will have developed this complication before death The extensive terature on this subject has been reviewed in detail by *Aastrup* whose results e in accord with those found in the present series

nterval between initial rheumatic infection and auricular fibrillation

As shown in Table 40 the interval between the initial rheumatic infection nd manifest auricular fibrillation was shorter than 10 years in only 2 out of 14 cases (2 per cent of the whole group) In 25 cases in all the arrhythmia t on after an interval shorter than 20 years (22 per cent) In 55 per cent of e group it was ascertained after an interval of less than 30 years in 84 per ent after less than 40 years in 97 per cent after less than 50 years and in ll cases within 60 years after the first rheumatic infection

TABLE 40

Interval between Initial Rheumatic Infection and Manifest Auricular Fibrillation

I 1 y	N f p t t	C m l t p t g
0–9	2	2
10–19	23	22
20–29	38	55
30–39	33	84
40–49	15	97
50–59	3	100
Total	114	

It appears that in 78 per cent auricular fibrillation was not ascertained until fter an interval of 20 years or more and in 45 per cent after an interval of 0 years or more Correspondingly the average interval between the initial heumatic infection and auricular fibrillation was 27 0 years

Interval between the first heart symptom and auricular fibrillation

The interval between the first heart symptom and manifest auricular fibrillation varied from 0 to 48 years

Table 41 shows that auricular fibrillation was ascertained in 66 out of 204 patients within 5 years after the first heart symptom (32 per cent of the whole group) In 54 per cent in all the arrhythmia was ascertained within 10 years after the first symptom in 67 per cent within 15 years in 79 per cent within 20 years and in 92 per cent within 30 years after the first symptom

TABLE 41
Interval between the First Heart Symptom and Auricular Fibrillation

Interval	No of patients	Cumulative percentage
0– 4 years	66	32
5– 9	45	54
10–14	26	67
15–19	23	79
20–24	15	86
25–29	12	92
30 years or more	17	100
Total	204	

The average interval between the first heart symptom and manifest auricular fibrillation was 10 6 years for the whole group

Interval between auricular fibrillation and right heart failure

The relation as to time between the occurrence of auricular fibrillation and right heart failure in the present series is given in Table 42

TABLE 42
Relation between Auricular Fibrillation and Right Heart Failure

Right heart failure before auricular fibrillation	9 patients
Right heart failure the same year as auricular fibrillation	73
Right heart failure later than auricular fibrillation	58
Right heart failure not ascertained later	66

Nine out of 206 patients with auricular fibrillation had right heart failure before the arrhythmia was ascertained and in 73 patients auricular fibrillation

nd right heart failure were ascertained the same year Thus 82 patients in ll (40 per cent) had right heart failure when auricular fibrillation was ascertained Of the 124 patients in whom auricular fibrillation was ascertained without simultaneous right heart failure 58 (79 per cent) developed definite right heart failure later in 27 after 1 to 4 years in 23 after 5 to 9 years and in 8 after more than 9 years In 66 patients with auricular fibrillation right heart failure was not ascertained later In 41 it had not been ascertained after to 4 years in 14 after 5 to 9 years and in 11 after 10 years or more

Auricular fibrillation was thus seldom preceded by manifest right heart failure but in a considerable number of cases it was ascertained simultaneously with right heart failure and in more than half the cases it was an earlier complication in the course of the disease than right heart failure

Survival after Auricular Fibrillation was first ascertained

The survival after auricular fibrillation was first demonstrated is shown in the survival curves for males and females separately in Fig 11

The survival curve for 148 females with manifest auricular fibrillation shows a fairly even fall with advancing age so that 62 per cent survived after 5 years 32 per cent after 10 years and 12 per cent after 16 years

Similarly the survival curve for 58 males shows that 43 per cent survived after 5 years 21 per cent after 10 years and 10 per cent after 16 years

Among females 50 per cent survived 6 to 7 years and among males 50 per cent survived 4 to 5 years

These survival times apply to the whole series including the so called terminal or fatal cases of auricular fibrillation Of these fatal cases only one

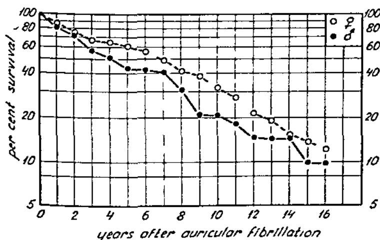


Fig 11
Survival after auricular fibrillation was ascertained

occurred with certainty in the present series in a woman aged 23 The series contained 13 cases of terminal auricular fibrillation the patients died in a few weeks with right heart failure and the following complications Subacute bacterial endocarditis in 1 case pneumonia in 3 cases arterial emboli in 9 and pulmonary emboli with infarction in 7 cases

Further 17 patients died within a year after auricular fibrillation had been ascertained one patient was under 20 years of age and also had right heart failure 10 had right heart failure when the arrhythmia was ascertained and died in heart failure without special complications 6 patients had no right heart failure when auricular fibrillation was diagnosed 3 of these died of cerebral emboli 1 of heart death (other details not available) and 9 died of affections other than cardio vascular disease

As the number of fatal and terminal cases of auricular fibrillation was not very large (7 per cent) these have not been considered separately in the survival calculation even though the survival times would have been slightly longer if these prognostically severe forms had been excluded

The literature on survival times after auricular fibrillation has been ascertained was thoroughly dealt with in *Aastrup*s thesis In a group of 47 cases *of rheumatic valvular disease in his own series he excluded cases with auri*cular fibrillation of fatal and terminal types cases under 20 years and deaths of other causes He then found that only one sixth died after 1 year about one third after 3 years and that almost half the patients survived 5 years or more after the onset of auricular fibrillation

These survival times correspond fairly well to the findings in the present series where as already mentioned the prognostically especially severe groups have not been excluded

In *Grant*s series of men in the armed forces a total of 33 per cent of 48 patients with auricular fibrillation and at the average age of 36 6 years were alive after 10 years This is approximately in accord with the survival percentage in the present series considering the high average age in this

Paroxysmal Auricular Fibrillation

Of the 206 patients included in the analysis above 16 had definite paroxysms of auricular fibrillation before it became chronic This number includes 11 out of the 144 patients who died and 5 out of the 62 surviving patients *In 10 cases* the diagnosis was based upon detailed description of the attacks and it was verified by electrocardiography in 6 cases The duration of the period of paroxysms could not be definitely stated in 5 cases in 6 the paroxysmal fibrillation became chronic in 10 years and in 5 cases after intervals varying from 10 to 23 years

In 2 out of the 24 surviving patients with sinus rhythm paroxysms of auri

cular fibrillation were ascertained A woman aged 43 has had such attacks for 3 years and a woman aged 55 for 14 years These two patients had sinus rhythm at the follow up

Paroxysmal auricular fibrillation was thus found in 18 out of 271 patients in the present series or in about 7 per cent and 16 of these patients later developed persistent auricular fibrillation

Paroxysmal Tachycardia

Paroxysmal tachycardia verified by electrocardiography was present in 5 patients 4 women at ages of 25 34 46 and 51 years and 1 man aged 43 This group represents 5 per cent of the patients with sinus rhythm at the first observation 3 patients developed chronic auricular fibrillation after 0–1 14 and 20 years the survival times after manifest paroxysmal tachycardia were 5 and 14 years in 2 of these patients who died and 21 years in one surviving case The fourth woman still had sinus rhythm with frequent attacks after 20 years The fifth patient died in heart failure after 1 year

Paroxysmal tachycardia verified by electrocardiography was thus a rare complication in the course of mitral stenosis in the present series and apparently does not seriously influence the prognosis

RIGHT HEART FAILURE IN THE COURSE OF MITRAL STENOSIS

Right heart failure is a frequent terminal stage during the usual course of mitral stenosis It may develop slowly and insidiously in many cases and it may therefore be difficult to fix the time when it was established This is seen especially in patients with auricular fibrillation treated regularly with digitalis In other cases various factors may cause right heart failure to become manifest this may for instance be seen in intercurrent infection of the respiratory tract in the case of some complication such as pulmonary embolism or acute auricular fibrillation or in the case of other physical stress such as pregnancy or physical over exertion

As mentioned on page 43 the criteria for right heart failure in the present work were *signs* of failure of the right side of the heart *ascertained on physical examination* i e enlargement of the liver ascites oedemas or visible venous congestion possibly supplemented by a measured venous pressure exceeding 12 cm of water A combination of several of these objective signs was considered necessary to recognize the presence of right heart failure and enlargement of the liver was demonstrated in all cases dealt with here the diagnosis of right heart failure must thus be considered fairly safe

In the following the age at the onset of right heart failure means the age at which this was first demonstrated With the definition used here it is obvious that the diagnosis of right heart failure will be dated later than the actual time of onset in several cases and that the calculated survival times will be too short On the other hand the data and survival times given will be more definite

Incidence of right heart failure in the present series

Of 271 patients 67 (25 per cent) presented right heart failure at the first examination In the course of the period of observation it was ascertained in 107 patients so that 174 patients in all presented this syndrome When 18 cases with insufficient data in this respect are excluded a total of 68 per cent of the present series had right heart failure

With regard to dead patients 141 out of 174 cases of mitral stenosis with sufficient data had right heart failure (81 per cent) Correspondingly *Graham et al* found 71 per cent with this syndrome among 100 patients with mitral stenosis who died

Age when right heart failure was ascertained

The distribution of the series according to age when right heart failure was first ascertained is given in Table 43

TABLE 43
Age when Right Heart Failure was ascertained

Age	No. of patients	Cumulative percentage
15–19 years	1	0 5
20–24	8	5
25–29	8	10
30–34	17	20
35–39	23	33
40–44	27	48
45–49	35	68
50–54	17	78
55–59	16	88
60–64	13	94
65–69	8	99 5
70–79	1	100
Total	174	

Only 1 patient had had right heart failure before the 20th year (0 5 per cent) 10 per cent in all had had right heart failure before the 30th year

33 per cent before the 40th year, 68 per cent before the 50th year, 88 per cent before the 60th year, and 99.5 per cent before the 70th year.

The average age when right heart failure was ascertained was 45.6 years.

Interval between initial rheumatic infection and onset of right heart failure

Table 44 gives a survey of the interval between the first rheumatic infection and the onset of right heart failure. It appears that 3 out of 102 patients developed right heart failure in the course of 10 years after the initial rheumatic infection. In 18 per cent in all the interval was shorter than 20 years, in 51 per cent shorter than 30 years, in 80 per cent shorter than 40 years, and in 96 per cent shorter than 50 years.

The average interval was 29.0 years.

TABLE 44

Interval between Initial Rheumatic Infection and Right Heart Failure

Interval	No. of patients	Cumulative percentage
0– 9 years	3	3
10–19	15	18
20–29	34	51
30–39	30	80
40–49	16	96
50 years or more	4	100
Total	102	

Interval between first heart symptom and right heart failure

Of 172 cases in which the time of onset of the first symptoms was known 42 (24 per cent) developed right heart failure within 5 years after the first symptom. 43 per cent in all developed right heart failure in the course of 10 years after the first symptom, 58 per cent in 15 years, 73 per cent in 20 years, and 89 per cent presented right heart failure 30 years after the first symptom had appeared (Table 45).

The average interval was 13.2 years.

It appears that a considerable number of patients developed right heart failure after a short period with symptoms: in all 24 per cent within 5 years and 43 per cent within 10 years after the first heart symptom.

TABLE 45

Interval between First Heart Symptom and Right Heart Failure

Interval	No of patients	Cumulative percentage
0– 4 years	42	24
5– 9	33	43
10–14	25	58
15–19	25	73
20–24	15	81
25–29	12	89
30–34	10	95
35–39	6	98
40 years or more	4	100
Total	172	

Relation between auricular fibrillation and right heart failure

Among the 174 patients with manifest right heart failure 131 in all (75 per cent) had auricular fibrillation 32 had definite sinus rhythm (19 per cent) whereas the rhythm was unknown in 11 cases (6 per cent)

The duration of auricular fibrillation in the 131 cases has been previously mentioned (page 115) In 58 patients it had been present for more than 1 year including 31 in whom it had persisted more than 4 years whereas auricular fibrillation and heart failure were ascertained in the same year in 73 patients Of the 32 patients with sinus rhythm 9 developed auricular fibrillation in from 1 to 3 years 23 patients had sinus rhythm till they died or at the time of the follow up

In the great majority of cases right heart failure was thus associated with auricular fibrillation

Survival Time after Development of Right Heart Failure

The survival curve for the 174 patients with right heart failure is shown in Fig 12

The curve shows an approximately linear decline 68 per cent survived 1 year 55 per cent 2 years 42 per cent 3 years 35 per cent 4 years 31 per cent 5 years 25 per cent 6 years 11 per cent 10 years and almost 6 per cent 12 years

50 per cent survived from 2 to 3 years (about 2 3 years)

The survival curve shows a more abrupt decline during the first year of observation than during the next years This finding is well known in the

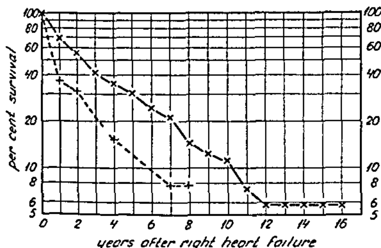


Fig 17
vival after development of right heart failure the longer curve represents all cases the shorter one cases with sinus rhythm

rature *11* per cent of cases of decompensated mitral valve disease in *Perl h*s series (*Perlroth* 1935) thus died in the first year and in *Davis and eiss*s series 50 per cent of cases of decompensated rheumatic valve disease d during this period

The median survival time of 2 3 years in the present series corresponds fairly ll to the statements in the literature In cases of decompensated mitral ste sis *Aastrup* thus gave an average duration of life of 1½ years *Grant* stated m 4 to 5 years *Stone and Feil* 3½ years and *Love and Levine* (1952) 3¼ rs In estimating these statements differences in the definition of the con t decompensated heart disease should be considered

ses with long survival times

It is of special interest that a group of 11 per cent of the present series ed 10 years or more with right heart failure The group comprised 9 pa nts 8 females and 1 male who may be briefly mentioned 5 out of the 9 tients had had rheumatic infection The heart symptoms set on between e 20th and 29th years in 3 patients between the 30th and 39th years in 5 d in the 48th year in the last patient Right heart failure had been ascer ned at ages from 37 to 60 years averaging 44 6 years All patients had ricular fibrillation at the time when heart failure was ascertained During e late course of the disease 4 patients had had arterial emboli and 2 had d pulmonary emboli The course of the disease had been characterized by e prolonged right heart failure but otherwise the clinical pictures had not

differed in particular from the other cases of mitral stenosis In 6 cases the arterial blood pressure did not exceed 150/90 mm Hg In the 3 other cases the highest values were 180/90 140/100 and 155/100 mm Hg at ages of 6 59 and 52 years

Four patients of this group died 10 10 10 and 11 years after right heart failure had been ascertained whereas 5 patients were still alive 10 11 14 15 and 16 years after this complication had developed In 3 cases a complicating tricuspid valve affection was considered but not definitely ascertained In 3 cases autopsy confirmed the diagnosis of mitral stenosis and neither showed signs of tricuspid valve affection at autopsy

Love and Levine (1952) pointed out that between 10 and 13 per cent of their cases of mitral stenosis lived 9 years or more after heart failure or auricular fibrillation had been clinically demonstrated On the basis of an analysis of 65 cases – four fifths with heart failure for an average period of 10 6 years and nine tenths with auricular fibrillation for an average period of 12 6 years the authors concluded that this group with a long survival time had a greater preponderance of females than series of mitral stenoses in general that the group attains a higher average age than the average of mitral stenoses but that otherwise it cannot be distinguished by special characteristics from the other cases of mitral stenosis The writer s experiences are in complete accord with *Love and Levine s* observations

Tricuspid valve disease had been diagnosed in 15 out of 65 cases in Love and Levine s series As already mentioned this diagnosis was considered in 3 cases of the present series but not definitely established

Heart rhythm and survival time

Fig 12 shows that the survival curve for 23 patients with persistent sinus rhythm during right heart failure is much lower than that of the whole group with right heart failure In cases with sinus rhythm the survival percentage falls below 50 within 1 year and is as low as 8 after 7 years The tendency a shorter survival time in the case of right heart failure with sinus rhythm than in auricular fibrillation was mentioned already in 1926 by *Parkinson and Clark Kennedy* they found an average survival time of 6 months in 15 cases *of rheumatic heart disease with sinus rhythm In Grant s series the* survival time in congestive failure in 21 cases with auricular fibrillation averaged 5 years as compared to an average survival of 2½ years in 24 cases with sinus rhythm (patients with subacute bacterial endocarditis who have a much shorter survival time not being considered here)

CARDIAC ASTHMA AND ACUTE PULMONARY OEDEMA IN ISOLATED MITRAL STENOSIS

In the literature on cardiac asthma and acute pulmonary oedema the procedure has often been to distinguish between cases in pregnant and non pregnant women Cardiac asthma and acute pulmonary oedema during pregnancy in mitral stenosis were recognized early and mentioned especially in French literature (*Pouliot* 1901 *Laennec* 1930)

Acute pulmonary oedema as a complication in isolated mitral stenosis without pregnancy was apparently first described in 1896 by *Hall* in a paper in The Medical Fortnightly in St Louis The case report was reproduced in *Vion's* thesis (Paris 1941) The patient was a man aged 21 who died in an attack of pulmonary oedema after only 3 weeks heart complaints The diagnosis of isolated mitral stenosis was verified at autopsy Acute pulmonary oedema in isolated mitral stenosis without pregnancy has however been rather unnoticed until *Gallavardin* in 1921 described 4 cases in women at ages from 35 to 52 years Since then the syndrome has been the subject for much discussion in French literature All the French cases and a few from other countries were dealt with in detail in 1941 in *Vion's* thesis which contains 47 case reports The clinical picture has also been described by *Schellong* (1933) *McGinn and White* (1934) *Fiedler* (1935) *Bramwell and Jones* (1944) and *Brett* (1948)

Cardiac asthma and acute pulmonary oedema in mitral stenosis have become of increasing interest during recent years as the presence of these symptoms is considered a special indication for mitral valvulotomy

Cardiac asthma and acute pulmonary oedema in the present series

As mentioned on page 43 the criteria according to which the presence of cardiac asthma or acute pulmonary oedema was recognized in the present series were as follows It was required that the case record contained a detailed description of attacks of dyspnoea with cough and copious frothy or bright red sputum possibly with an admixture of a small quantity of fresh blood associated with impaired general health and of 15 to 30 minutes duration (cardiac asthma) or lasting 1 hour or more (acute pulmonary oedema) In the following the two complications are dealt with as a whole

Incidence of cardiac asthma and acute pulmonary oedema

In the present series 45 out of 271 patients (17 per cent) had cardiac asthma or acute pulmonary oedema In *Aastrup's* series the syndrome was present in 11 out of 50 cases of mitral stenosis (22 per cent) Otherwise the incidence of these complications in mitral stenosis is not mentioned in comparable series of cases strangely enough *Grant* does not mention the syndrome

In a series of cases of mitral stenosis operated on *Logan and Turner* (1953)

found acute pulmonary oedema in 17 out of 100 patients *Brock et al* (19)[n] in 6 out of 50 patients but both were series of selected cases which cannot be directly compared with the present series

Sex and age

The present series comprises 34 females and 11 males The ratio between females and males is thus 3 1 1 i e a somewhat greater preponderance of women than in the total series where the corresponding ratio is 2 5 1

TABLE 46
Sex and Age Inciden c at the First Attack of Cardiac Asthma and Acute Pulmonary Oedema

	15–19	20–29	30–39	40–49	50–59	60–69 y	Total
Females	1	10	9	10	3	1	34
Males	1	3	2	3	2	–	11
Total	2	13	11	13	5	1	45

The age incidence at the first attack of cardiac asthma or acute pulmonary oedema is shown in Table 46 It appears that the first attack occurred in 9 patients before the 20th year in 13 between the 20th and 29th years in 11 between the 30th and 39th years in 13 between the 40th and 49th years in 5 between the 50th and 59th years and in 1 patient after the 60th year

The average age at the first attack was 37 4 years

Condition before the first attack

All patients except one had had heart complaints before the first attack of cardiac asthma or acute pulmonary oedema In 19 patients the symptoms had persisted less than 5 years in 10 from 5 to 9 years in 7 from 10 to 14 years in 5 from 15 to 19 years and in 3 patients more than 20 years before the first attack The average duration of symptoms before the first attack was 7 5 years

Condition at the first attack

The *heart rhythm* at the first attack is known in 36 cases 23 had sinus rhythm 1 probably had paroxysmal tachycardia 1 had paroxysmal auricular fibrillation (verified by electrocardiography) and 11 had chronic auricular fibrillation Thus almost two thirds had sinus rhythm at the first attack

QRS axis – Judged by the electrocardiogram taken at the first examination 17 out of 45 patients (38 per cent) of this group had right axis deviation

according to the criteria previously mentioned In the rest of the series 29 per cent had right axis deviation

Size of the heart – Roentgenologic examination of the heart had been performed soon after the first attack in 36 patients 6 of this group had a cardiothoracic index under or equal to 50 13 had an index between 51 and 54 13 between 55 and 64 and in 2 cases the index was over 64

Right heart failure – This was present at the first attack in 11 patients including 9 with chronic auricular fibrillation

Factors provoking attacks

Severe physical exertion released the attacks in 12 patients Emotion decidedly released the attacks in 2 cases In 4 patients they occurred during pregnancy (2 cases) or in the course of delivery (2 cases)

The attacks were released in 2 patients during tachycardia in 1 probably during an attack of paroxysmal tachycardia as already mentioned and in the other case in the course of a verified attack of paroxysmal auricular fibrillation

In 37 patients the attacks were most pronounced by day in 8 they were only nocturnal

It has been mentioned often in the literature (*Vion* 1941 *McGinn and White* 1934 *Gallavardin* 1921) that the attacks are released by sexual intercourse or in conjunction with menstruation No such relation has been observed in the present series

Frequency of attacks

This is not fully known but it may be mentioned from the available data that 12 patients had had only 1 attack during which 6 died 3 patients had had only 2 attacks The remaining 30 patients had all had more than 2 attacks at least 7 of these patients had had more than 10 attacks

Course of the Disease after the First Attack

Thirty four patients of the whole series died during the period of observation and 11 were alive at the time of the follow up

(1) Deaths during period of observation

Nine patients in all died of acute pulmonary oedema including 6 who died during the first attack All were women aged 19 24 35 35 41 and 46 when they died 3 of these patients had right heart failure before the attack and 5 in all of this group had auricular fibrillation before the attack The sixth patient had sinus rhythm but had increasing dyspnoea on exertion during the year before the attack In all 6 cases symptoms thus suggested some progression of the heart disease before the fatal attack of acute pulmonary oedema

3 patients died during a subsequent attack of pulmonary oedema 9 5 and 10 years respectively after the first attack The ages at death in these cases were 24 33 and 34 years

Further 18 patients died of the heart disease without pulmonary oedema 15 of this group died of congestive failure after 0-1 0-1 2 2 2 3 5 6 8 8 8 11 14 15 and 17 years 2 patients died of heart death after 4 and 6 years and 1 patient suddenly died 6 years after the first attack

One patient died of recurrence of rheumatic fever 6 years after the first attack

Two patients died of pneumonia after 0-1 and 1 year and 4 patients died of cerebral emboli after 1 2 5 and 16 years

Age at death – The youngest patient died at the age of 19 6 between the 20th and 29th years 6 between the 30th and 39th years 10 between the 40th and 49th years 7 between the 50th and 59th and 4 between the 60th and 69th years The average age at death was 43 6 years thus somewhat lower than the average age at death in the whole series 47 0 years

The average survival time after the first attack of cardiac asthma or acute pulmonary oedema was 5 5 years in the case of those who died

(2) *Survivors*

At the time of the follow up 11 patients 7 females and 4 males were alive

The survival times after the first attack of cardiac asthma or acute pulmonary oedema were 2 8 9 10 14 15 and 18 years in the case of the women At the follow up 5 still had a tendency to attacks after 2 8 9 10 and 14 years whereas 2 had no attacks and had survived 15 and 18 years after the first 6 out of the 7 females had right heart failure at the follow up

The survival times in the case of males were 2 4 4 and 6 years They all had a tendency to attacks and 1 had right heart failure at the follow up

The average age of the surviving patients was 41 2 years The survival time after the first attack averaged 8 4 years

Total assessment of survival after the first attack

In assessing the survival after the first attack of cardiac asthma or acute pulmonary oedema it is reasonable to exclude patients who died during the first attack as an estimate of the long term prognosis will only be of importance after the first attack Fig 13 shows the survival curves for all cases surviving the first attack

The survival curve for the whole series shows a fairly even fall during the first 16 years 68 per cent surviving 5 years 37 per cent 10 years and 19 per cent 16 years The median survival time was 6 to 7 years

With regard to the patients who were under 50 years of age at the first

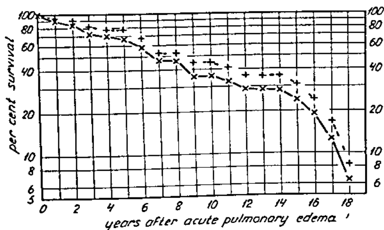


Fig 13

Survival curves for 39 patients with past first attack of cardiac asthma or acute pulmonary oedema The lower curve represents the whole group the upper refers to patients under 50 years

attack it appears that the survival curve is at a slightly higher level but otherwise closely follows that of the whole series In this group 78 per cent survived 54 years 46 per cent 10 years and 25 per cent 16 years The median survival time was 8 to 9 years

Discussion

With regard to sex and age incidence the present series is in accord with *Vion* s previously mentioned collective series from the literature which also included *Gallavardin* s cases of *retrecissement mitral oedemateux* It can thus be confirmed from the present series of cases that cardiac asthma and acute pulmonary oedema constitute a complication in mitral stenosis most frequently setting on at a comparatively early stage of the disease though also occasionally during the later course

Some of the patients of the present series have had only few attacks followed by a prolonged period without attacks whereas others have had attacks for years Both types occur in *Vion* s series

Single cases of death during an attack of cardiac asthma or acute pulmonary oedema have been described in the literature (*Schellong McGinn and White Gallavardin*) In *Vion* s collective series however only 4 deaths occurred among 47 cases described (8 per cent) and *Vion* concluded that the attacks apparently did not aggravate the general course of mitral stenosis However his series was not followed up

In the present series 6 patients died during the first attack of acute pulmonary oedema This corresponds to 3 per cent of all deaths during the period

of observation it must therefore be concluded that the risk of unexpected deat in acute pulmonary oedema was found to be very low in the present series

Three out of 39 patients with a past first attack of cardiac asthma or acu pulmonary oedema (8 per cent) died later in acute pulmonary oedema N does this finding seem to imply a great risk of death in acute pulmonary oedem for patients with past attacks

When the 9 patients who died of acute pulmonary oedema are left out consideration it appears that 25 patients died during the period of observatio and 11 survived Of the 25 deaths 18 died of heart failure (72 per cent) 1 rheumatic fever (4 per cent) 2 of pneumonia (8 per cent) and 4 of cerebr emboli (16 per cent) i e of causes with the same distribution as in the tot series of deaths 7 out of 11 survivors developed right heart failure during th period of observation and thus showed signs of progression of the mitr stenosis but the period of observation was long for some of these patients

The influence of the attacks of cardiac ashma and acute pulmonary oedem on the progression of the heart disease as a whole cannot be assessed as the exists no series that can be used for comparison

The average age of patients of this group who died was lower than th found in the total series similarly the average age of survivors was lower tha that in the whole group of survivors

It must therefore be concluded that cardiac asthma and acute pulmona oedema occurred in one sixth of the present series and were complicatio mostly in the early course of mitral stenosis They were seldom fatal but th group had a somewhat poorer prognosis with regard to duration of life tha the whole series of mitral stenosis

HAEMOPTYSIS IN MITRAL STENOSIS

The occurrence of haemoptysis in mitral stenosis has long been known I the Scandinavian literature the symptom has been mentioned by *Warburg* wh published in 1931 4 cases of mitral stenosis with early haemoptysis It appear from this publication that the patients had been suspected of pulmonary tuber culosis for some time before mitral stenosis was recognized *Oppenheimer an Schwartz* (1934) *Guzzetti and Dinkler* (1938) *Breu* (1948) *Thompson and Ste wart* (1951) and *Isaacs et al* (1953) have later contributed to the descriptio of haemoptysis in mitral stenosis

Haemoptysis in the present series

Pure blood was coughed up in 76 out of 271 cases (27 per cent) of the presen series

The incidence of haemoptysis in mitral stenosis varies rather much in the literature according to the nature of the series examined and the criteria of haemoptysis *Oppenheimer and Schwart* (1934) found only 3 cases of large haemoptysis among 1000 of mitral stenosis In *Wolff and Levine*s series haemoptysis occurred in 50 out of 541 cases (9 5 per cent) *Gray and Hunt* (19?8) found haemoptysis in 22 per cent of 75 patients and *Willner* (1930) gave an incidence of 39 per cent in 95 Chinese patients with mitral stenosis A higher incidence has been found in series selected for operation *Brock et al* (195?) thus found haemoptysis in 20 out of 50 patients *Logan and Turner* (19?3) in 17 out of 100 cases of mitral stenosis

Survey of the present series

Only cases in which it has been described that the patient undoubtedly coughed up pure blood have been included in this group It was analysed especially with a view to the circumstances under which the first haemoptysis occurred According to the available data it appeared that the first haemoptysis occurred in 16 cases in conjunction with cardiac asthma or acute pulmonary oedema in 29 cases it was a symptom in pulmonary infarction and in 31 cases an isolated haemoptysis occurred

A distinction between the three clinically different groups would of course be somewhat doubtful The groups cardiac asthma or acute pulmonary oedema and pulmonary infarction only include cases in which the description of the attack was sufficiently characteristic The group isolated haemoptysis is thus one of remainders and may possibly include cases belonging in either of the other groups Especially with a view to the long term prognosis it was never theless considered of interest to maintain the group of isolated haemoptysis and to analyse this in the same manner as those of cardiac asthma or acute pul monary oedema and pulmonary infarction

A survey of ages at the first haemoptysis in all groups is given in Table 47

TABLE 47

A e Incidence at the First Haemoptysis in Isolated Mitral Stenosis

I G p	d 0	) 9	30-39	40–49	50 9	60 69 y	T t l
Isolated haemoptysis	6	13	6	5	1	–	31
Haemoptysis n cardiac asthma or acute pumonary oedema	1	7	3	5	–	–	16
Haemoptysis in pulmonary infarction	–	4	8	7	9	1	9
Total	7	4	17	17	10	1	76

In the group of isolated haemoptysis the great majority of patients wa
under 40 years and the average age at the first attack was 29 2 years In th
group of cardiac asthma or acute pulmonary oedema the average age was 3?
years and in that of haemoptysis in pulmonary infarction the age average
42 6 years and was thus distinctly higher than in the two other groups

Isolated Haemoptysis

This group will be dealt with in greater detail reference being made to th
sections on cardiac asthma or acute pulmonary oedema and on pulmonary in
farction as far as the other groups are concerned

The series of isolated haemoptysis comprises 31 patients 19 females and 1
males

Condition before the first attack

Haemoptysis was the first symptom of mitral stenosis in 4 cases In 1
patients the heart symptoms had been present for less than 5 years in 8 fro
5 to 9 years and in 6 patients for more than 10 years The average duratio
of symptoms before the first haemoptysis was 5 4 years

Condition at the first haemoptysis

The heart rhythm when the first haemoptysis occurred is known in 26 pa
tients 4 with auricular fibrillation and 22 with sinus rhythm

Right heart failure was present in only 1 patient whereas 27 showed n
definite signs hereof

Factors provoking haemoptysis

Physical exertion released haemoptysis in 6 patients In 3 cases the haem
optysis occurred during pregnancy

Frequency of haemoptyses

Ten patients had only one haemoptysis and further 4 patients had only on
haemoptysis but 2 later developed acute pulmonary oedema and 2 pulmonar
infarction

Seventeen patients had 2 or more haemoptyses The absolute number of at
tacks is not known with certainty During the later course of the disease 6
patients developed attacks of cardiac asthma or acute pulmonary oedema (4
cases) or pulmonary infarction (2 cases) whereas 11 cases did not present such
complications

Course of Disease after the First Haemoptysis

Twenty three patients died during the period of observation 8 were alive
at the time of the follow up

(1) *Deaths during period of observation*

Deaths from haemoptysis did not occur in the present series

Thirteen out of 23 patients died of congestive failure and the survival times after the first haemoptysis in these cases were 1 2 4 4 4 5 7 7 11 16 23 25 and 37 years 1 patient died in acute pulmonary oedema 6 years after the first haemoptysis 2 died of pulmonary embolism 1 and 5 years after the first haemoptysis 2 died of cerebral embolism 5 and 28 years after the haemoptysis 1 patient died of pneumonia 28 years after the haemoptysis 2 died of sub acute bacterial endocarditis 2 and 7 years after the haemoptysis 1 patient died of recurrent rheumatic fever 6 years after the haemoptysis and 1 died of a different cause 4 years after the haemoptysis

The average age of all patients who died was 39 3 years The average survival time after the first haemoptysis in this group was 9 7 years

(2) *Patients surviving at the follow up*

Two out of the 8 survivors were well compensated at the time of the follow up and had survived 13 and 43 years after the first haemoptysis 6 patients had right heart failure and had survived 4 6 10 21 and 22 years after the first haemoptysis

The average age of survivors was 44 6 years the average survival time after the first haemoptysis 21 3 years

Total assessment of survival after the first haemoptysis

The survival curve for all cases of isolated haemoptysis is given in Fig 14 Counting from the time when the first haemoptysis occurred 74 per cent

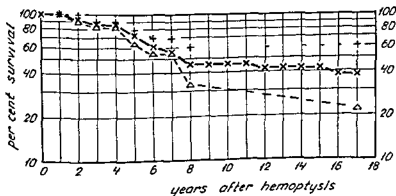


Fig 14

Survival after isolated haemoptysis The centre curve represents the whole group (31 patients) below the curve for 11 patients with recurrent haemoptysis above the curve for 10 patients with one haemoptysis

survived after 5 years 46 per cent after 10 years and 38 per cent after 16 years The median survival time of the whole group was 7 to 8 years

It has been attempted to demonstrate the importance of recurrent haemoptysis to survival in the lowest curve in Fig 14 It shows a somewhat greater fall in the survival in the group with recurrent haemoptysis as only about 30 per cent survived after 10 years and 22 per cent survived after 16 years

In contrast with this the survival curve for patients with one haemoptysis, the uppermost one in Fig 14 shows a less pronounced fall of the survival percentage in the course of time as 60 per cent of this group survived after 16 years

There was thus a tendency to a lower survival rate in recurrent haemoptysis, though it should be borne in mind that the two groups compared were small comprising only 11 and 10 patients respectively

Discussion

In most cases of the present series with isolated haemoptysis it was an early complication during the course of mitral stenosis The symptom occurred in 25 out of 31 patients before the 40th year in 4 cases it was the first symptom of mitral stenosis and in most cases it occurred a few years after the onset of the heart symptoms Auricular fibrillation when the first haemoptysis occurred was present in only 4 out of 26 cases in which all details were available and right heart failure occurred in only 1 out of 28 cases with available data

This finding is in accord with the statements in the literature (*Warburg* 1931 *Gui etti and Dinkler* 1934 *Breu* 1948)

In 14 cases haemoptysis was observed only once in 17 it was recurrent 10 cases in all were complicated later by acute pulmonary oedema or by pulmonary infarction It may be pointed out that severe loss of blood in haemoptysis did not occur in the present series

Deaths caused by haemoptysis in mitral stenosis did not occur in the present series A few deaths have been reported in the literature (*Isaacs et al* 1953 *Stewart* 1934) but cases of this nature are rare and no survey exists of the frequency of deaths from haemoptysis in larger series of mitral stenoses

It therefore seems justifiable to conclude that death caused by haemoptysis is very rare in mitral stenosis

In the whole group of cases with isolated haemoptysis the average age at death was 39 3 years in the present series i e lower than the average age at death in the whole series The age of survivors with haemoptysis averaged 44 6 years thus also lower than the average age of all survivors

The course of mitral stenosis both in patients who died and in survivors was characterized by progression of the heart disease with frequent development of right heart failure and in most fatal cases the patients died in congestive failure

Isolated haemoptysis was thus most frequently a symptom in the early course of mitral stenosis and it was never fatal With regard to duration of life the prognosis in these cases was a little less favourable than in most cases of mitral stenosis

PULMONARY EMBOLISM WITH PULMONARY INFARCTION

The occurrence of emboli in the pulmonary arteries with development of pulmonary infarction is a frequent complication in mitral stenosis

As previously mentioned the criteria according to which the diagnosis of pulmonary emboli with pulmonary infarction was established in the present series were clinical pictures with acute onset of dyspnoea cough stitch blood tinged expectoration fever and signs of pleurisy or pulmonary infiltration In rarer cases acute dyspnoea followed by a prolonged rise of temperature *signs* of pleurisy or pulmonary infiltration tachycardia possibly jaundice and no response to antibiotic treatment Furthermore as mentioned below this series includes a few cases diagnosed at autopsy

However as it has been pointed out recently by *Logan and Turner* it may be difficult in some cases of mitral stenosis to distinguish between pulmonary infarction and pure haemoptysis of other causation It can therefore undoubtedly be assumed that not all cases of pulmonary infarction have been diagnosed in the present series and that a few cases may have been included in the group of isolated haemoptysis The reason why a distinction between these two groups was nevertheless maintained was that these two complications showed a distinct difference with regard to the phase of the disease during which they occurred and with regard to the immediate and the late prognosis

The uncertainty in defining pulmonary infarctions is further increased by the fact that bedridden patients with mitral stenosis with pronounced heart failure rather often develop large pulmonary infarctions which do not produce characteristic clinical symptoms this has been emphasized especially by *Levine and White* (1937)

Occurrence of pulmonary infarction in the present series

Fifty five out of 271 patients (20 per cent) had had pulmonary infarction

Correspondingly *Aastrup* found pulmonary emboli in 18 out of 90 cases of mitral stenosis (20 per cent)

Fifty out of 189 patients with mitral stenosis who died had had pulmonary infarction (27 per cent)

Diagnosis in the present series

Of 70 pulmonary infarction episodes 65 had been clinically diagnosed haemoptysis had been present in 41 of these cases In 23 cases the clinical

diagnosis of a first or subsequent pulmonary infarction had been verified at autopsy

In 5 cases the diagnosis of pulmonary infarction was not established until at autopsy They were all patients with intractable heart failure in whom there had been no distinct clinical signs of pulmonary infarction

Condition at the first pulmonary infarction

Age and sex – The 55 patients are distributed on 37 females and 18 males The age and sex distribution at the first pulmonary infarction is shown in Table 48

TABLE 48
Age and Sex at First Pulmonary Infarction in Isolated Mitral Stenosis

	20–29	30–39	40–49	50–59	60–69 years	Total
Males	2	6	6	3	1	18
Females	4	5	16	9	3	37
Total	6	11	22	12	4	55

The earliest pulmonary infarction occurred in the age group 20–29 years and 17 patients in all had their first pulmonary infarction before the 40th year (30 per cent) The highest frequency is seen in the age group 40–49 years with 22 cases (40 per cent) after the 50th year there were 16 cases in all (30 per cent)

The average age at the first pulmonary infarction was 45 1 years

Cardiac state

(1) *Auricular fibrillation* – When the first pulmonary infarction developed 38 patients had unquestionable auricular fibrillation 14 had sinus rhythm and in 3 cases the rhythm was not known Auricular fibrillation was thus present in 70 per cent and was most frequent in patients over the 40th year as shown in Table 49

(2) *Right heart failure* – Right heart failure was present in 36 out of 55 patients (65 per cent) fairly evenly distributed on the age groups

(3) *Size of the heart* – Roentgenograms taken in close connection with the pulmonary infarction were available in 40 cases In 2 patients the cardio thoracic index was under 50 in 9 it was 51–54 in 28 between 55 and 64 and in 1 patient the index was over 64

TABLE 49

Clinical State at First Pulmonary Infarction in 55 Cases of Mitral Stenosis

	Total	Right heart failure	Heart rhythm		
			Sinus rhythm	Auricular fibrillation	Rhythm unknown
20–29 years	6	2	4	2	0
30–39	11	7	6	5	0
40–49	22	17	2	18	2
50–59	12	6	2	9	1
60–69	4	4	0	4	0
Total	55	36	14	38	3

Special factors predisposing to pulmonary infarction

Subacute bacterial endocarditis was definitely ascertained in 1 patient and its presence was supposed in another patient Both were women between 20 and 29 years 2 patients developed pulmonary infarction after appendectomy and 1 after abortion Finally 1 patient had phlebitis of the lower extremities

Summing up it can thus be ascertained that pulmonary infarction occurred at an average age of 45 1 years in the present series that 70 per cent of the patients had had auricular fibrillation 65 per cent right heart failure and that 29 out of 40 patients examined had cardio thoracic indices over 54 Pulmonary infarction was thus in most cases a late complication during the course of mitral stenosis

Recurrences of pulmonary infarction

Recurrence of pulmonary infarction was seen in 14 out of 28 patients who survived the first attack (50 per cent) 11 of these had only one recurrence 3 had several

Findings at autopsy

Of 85 autopsied cases of mitral stenosis 28 had fresh pulmonary infarctions (33 per cent) this corresponds to the frequency of 31 per cent of pulmonary infarctions in 101 cases of mitral stenosis reported by *Graham et al* and to 31 per cent in *Levine and White* s 52 autopsied cases

Thromboses in the right atrium in pulmonary infarction were found in 6 out of 15 autopsied cases of the present series Correspondingly *Graham et al* found thromboses in the right atrium in 9 out of 31 cases of mitral stenosis with pulmonary infarction

Course of Disease after Development of Pulmonary Infarction

(1) *Patients who died during the period of observation* – 50 patients of this group died 5 were alive at the time of the follow up

Of the whole group of 55 patients 27 (49 per cent) died soon after the first attack of pulmonary infarction

Of the clinically diagnosed cases 22 out of 50 (44 per cent) died soon after the first attack

Fourteen out of the 28 patients who survived the first attack (50 per cent) later had one or several recurrences and 10 patients died immediately after a recurrence The survival times of these patients after the first attack were 0–1 1 2 2 2 4 5 5 10 and 16 years

Thus 32 in all out of the 50 patients with clinically diagnosed pulmonary infarction (64 per cent) died soon after this complication Since as previously mentioned there were several contributory causes of death in many cases pulmonary infarction was not the actual cause of death in all these cases In 14 cases in all it was considered the actual cause of death whereas it was contributory in the other cases

Thirteen patients died without pulmonary infarction as contributory cause 11 of congestive failure and 2 of arterial emboli The survival times in these cases were 0–1 0–1 0–1 0–1 2 3 4 4 6 7 7 12 and 18 years

The average age for all patients who died was 47 0 years i e the same as in the whole series

(2) *Patients surviving at the time of the follow up*

Five patients were alive at the follow up 4 with right heart failure The average age was 54 2 years The survival times after the first attack were 0–1 2 11 15 and 16 years

Assessment of survival after the first pulmonary infarction

Twenty two out of 50 patients with clinically diagnosed pulmonary infarction died soon after the first attack Patients who developed pulmonary infarctions thus had a very serious prognosis in the present series

The survival among patients surviving the first pulmonary infarction is shown in Fig 15 It appears from the survival curve that 46 per cent survived 5 years 27 per cent 10 years and 11 per cent 17 years The prognosis for patients who survived the first pulmonary infarction was thus also serious in the present series

Summary

Pulmonary infarction was a complication developing late during the course of mitral stenosis in the present series The average age at the first attack was 45 1 years 70 per cent of the patients had auricular fibrillation 65 per

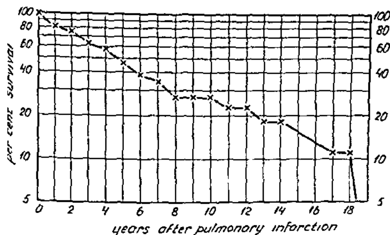


Fig 1
Survival curve for 98 patients who survived the first pulmonary infarction

cent had right heart failure and 28 out of 40 cases in which roentgenograms were available had a cardiothoracic index over 54

The pulmonary infarctions thus occurred in patients who already had an advanced mitral *stenosis*

The prognosis in cases with clinically diagnosed pulmonary infarction was very serious 44 per cent died soon after the first attack Among those who survived the first attack the survival percentage was 46 after 5 years 27 after 10 years and 11 after 17 years Fifty per cent of the survivors had one or several recurrences of pulmonary infarction

With regard to duration of life this group corresponds to the average found in the whole series of cases of mitral stenosis

OTHER PULMONARY AFFECTIONS DURING THE COURSE OF MITRAL STENOSIS

Of other pulmonary affections mention may be briefly made of pneumonia and haemosiderosis

Pneumonia

It is a well known fact that patients with mitral stenosis are especially pre disposed to infections of the respiratory tract The present series contained numerous cases with acute or chronic bronchitis in the past history but these statements can hardly be considered complete and the frequency of this com plication will not be assessed

Pneumonia was described in 97 cases (36 per cent) including 24 with re peated pneumonia

This complication occurred at any time during the course of the disease but as might be expected most frequently during the last phase As previously mentioned pneumonia was the cause of death in 3 per cent of the cases It is worthy of mention here that before chemotherapeutics and antibiotics were introduced pneumonia undoubtedly contributed to a permanent aggravation in a great number of the more advanced cases of mitral stenosis With the modern effective treatment of pneumonia the shortened course of this disease may be expected in the course of time to result in an improvement of the prognosis of mitral stenosis

Haemosiderosis in the lungs

It is well established that the roentgenogram of the lungs in mitral stenosis may on rare occasions show pulmonary haemosiderosis as a diffuse widespread micronodular process which may be exactly like the roentgenologic findings in Boeck s disease miliary tuberculosis pneumoconiosis or carcinomatosis

In the Scandinavian literature this finding has been mentioned by *Arseth* (1948) and by *Frost et al* (1952) The latter authors reported 4 cases of pul monary haemosiderosis in mitral stenosis 3 of these cases were histologically verified as haemosiderosis as deposits of haemosiderin were demonstrated in the macrophages of the pulmonary tissue The existing literature on haemo siderosis in the lungs has been reviewed by *Frost et al Lendrum et al* (1950) and by *Laubry et al* (1948) It appears from these publications that roentgeno logically demonstrable haemosiderosis in the lungs in mitral stenosis is most frequent in males between 20 and 40 years of age that it may be present both with mild and with severe symptoms and that it is relatively frequent in con junction with repeated haemoptysis

The incidence of roentgenologically demonstrable *haemosiderosis in the* lungs in mitral stenosis has not been precisely established

In the present series a study of 189 cases showed roentgenologically verified haemosiderosis in the lungs in only 1 case The patient was a man He had had no rheumatic infections stated that he had had heart symptoms from his 23rd year and from that time repeated attacks of acute pulmonary oedema durin which he coughed up small quantities of pure blood At the first observation he was 27 years had sinus rhythm and presented signs of right heart failure The electrocardiogram showed right axis deviation and a negative T_3 *The cardio thoracic index* was 62 and the vascular markings of the lungs showed in the roentgenogram a diffuse micronodular pattern characteristic of haemo siderosis He had increasing heart trouble after the first examination and died 1 year later in his home in complete heart failure

Roentgenologically demonstrable haemosiderosis in the lungs was thus observed in only 1 out of 189 cases in the present series and the findings in this case were in accord with the statements in the literature

ARTERIAL EMBOLI IN THE SYSTEMIC CIRCULATION IN MITRAL STENOSIS

The occurrence of arterial emboli in the systemic circulation is such a frequent and momentous complication in mitral stenosis that special mention of this was considered justifiable

There is a very extensive literature on the subject A survey of the publications has been given by *Lenegre et al* (1951) The authors themselves mentioned 100 cases of cerebral emboli in mitral disease Among the more important publications of recent years mention may be made of *Harris and Levine* s survey of 72 cases of cerebral emboli in mitral stenosis (1941) and of one by *Daley et al* (1951) comprising 194 cases of arterial emboli in rheumatic heart disease (almost exclusively mitral disease)

Arterial emboli in the systemic circulation in the present series

Arterial emboli in the systemic circulation occurred in a total of 75 patients of the present series (28 per cent of the whole series) Of the 189 dead patients 61 in all had had arterial emboli (32 per cent)

Clinical features

This group comprised 22 males and 53 females the ratio females/males thus being 2 4 1 which is in accord with the usual sex incidence in the total series

The age distribution when the first arterial emboli occurred is shown in Table 50 there is a distinct predominance of females and the highest incidence is in the age group 40–49 years

TABLE 50

Age and Sex Incidence when Arterial Emboli First Occurred in the Systemic Circulation

	20–29	30–39	40–49	50–59	60–69	70–79 y	Total
Males	3	[illegible]	[illegible]	5	[illegible]	–	22
Females	5	7	19	17	4	1	53
Total	8	12	26	2	6	1	75

Arterial emboli in the systemic circulation were not observed until the 20th year in the present series 8 patients had their first emboli before the 30th year and 20 before the 40th year (27 per cent) 26 patients (33 per cent) had their first emboli between the 40th and 49th years In 22 cases in all the complication developed between the 50th and 59th years in 6 between the 60th and 69th years and in 1 after the 70th year

The average age when the first arterial emboli developed was 45 ? years

Localization of the emboli

A survey of the localization of the arterial emboli in the present series is given in Table 51 As the present book deals with the clinical conditions the diagnoses of emboli given in the table are based solely upon the *clinical* findings Discrepancies between the clinical and the pathologic anatomical diagnosis of emboli will be mentioned in the section on autopsy findings

The most frequent form of arterial emboli in the systemic circulation appeared to be cerebral emboli which represented 60 per cent in all of the total number of arterial emboli Almost 2 per cent were localized to retinal arteries the rest being actual cerebral emboli

The second most frequent form is arterial emboli in the lower extremities representing 22 per cent of all emboli

Emboli in arteries to the abdominal organs constitute the third largest group representing 12 per cent of all emboli The group comprises emboli in splenic renal and mesenteric arteries

Rarer forms were emboli in the upper extremities 4 per cent of all and in the aorta and the iliac arteries 2 per cent of all

Number of embolic episodes and interval between these

Different localizations of arterial emboli were comparatively frequent in the same patient within a period of a few hours or days For practical reasons all arterial emboli occurring within a week were considered one embolic episode According to this arbitrary definition 47 patients have had 1 embolic episode whereas 28 have had repeated episodes varying from 2 to 6 24 patients have had 2 episodes 2 have had 3 1 has had 4 and 1 has had 6 episodes

The interval between repeated episodes varied from 1 week to 10 years In 4 patients the second episode occurred within a year in 24 after more than 1 year and in 7 of these after more than 5 years

Cardiac state when the first arterial emboli occurred

(1) *Auricular fibrillation* –

With regard to the heart rhythm when the first arterial emboli occurred reliable data were available in 67 out of 75 cases 57 patients had auricular

TABLE 51

Localization of 123 Emboli in 75 Patients

Localization		No. emboli	
Arteries to the brain –		74	60
Cerebral arteries	72		
Retinal arteries	2		
Arteries to abdominal organs –		15	12
Splenic artery	7		
Renal arteries	7		
Mesenteric arteries	1		
The aorta and iliac arteries		2	2
Arteries to the lower extremities		27	22
Arteries to the upper extremities		5	4
Total		123	100

fibrillation (85 per cent of the part of the series in which definite data were available) As far as it can be ascertained 10 patients (15 per cent of those with reliable data) had sinus rhythm when the first arterial emboli developed As not all patients were observed just at the time when embolism occurred the possibility cannot of course be excluded that some may have had paroxysmal auricular fibrillation at that time

TABLE 52

Heart Rhythm when First Arterial Emboli Occurred in Mitral Stenosis

	20–29	30–39	40–49	50–59	60–69	70–79 y	Total
Auricular fibrillation	6	10	19	16	5	1	57
Sinus rhythm	2	1	5	2	–	–	10
No data available	–	1	2	4	1	–	8
Total	8	12	26	22	6	1	75

Table 52 gives a survey of age and heart rhythm when the first arterial emboli occurred It appears that patients with sinus rhythm were chiefly to be found in the age groups under 50 years but also that the incidence of auricular fibrillation was high in all age groups

The duration of auricular fibrillation before the first embolic episode i known in 56 cases 1 patient developed embolism in the course of paroxysma fibrillation 15 patients had had auricular fibrillation for less than 1 year 1! for periods from 1 to 4 years 15 for periods from 5 to 9 years and 6 patient had had auricular fibrillation for periods from 10 to 15 years Apparently ther is thus no relationship between the duration of auricular fibrillation and th occurrence of arterial emboli

(2) *Heart size* –
Roentgenologic assessment of the size of the heart in immediate connectior with the embolic episode was performed in only 16 patients 3 had a cardio thoracic index under 54 In 10 it varied from 55 to 64 and in 3 patients the index was larger than 65 The left atrium was enlarged in 13 patients slightly enlarged in 3 moderately enlarged in 9 and much enlarged in 1 patient

(3) *Right heart failure* –
Right heart failure diagnosed by the usual criteria was present in 26 patients (34 per cent) Its duration was known in 25 cases 9 out of the 25 had devel oped their heart failure within the year preceding the embolism 10 had had right heart failure for periods from 1 to 4 years 5 for periods from 5 to 9 years and 1 patient for 14 years

(4) *Drugs* –
Maintenance treatment with digitalis was instituted in 35 cases when the first emboli occurred The great majority of the patients had been given digi talis for several years and no relation between the digitalis therapy and the occurrence of arterial emboli could be demonstrated 1 patient developed em boli in the kidneys in the right iliac artery and the right posterior tibial artery in the course of quinidine treatment to convert auricular fibrillation into sinus rhythm Quinidine was however used in so few cases in the present series that a critical estimate of the risk of embolism when this drug is used cannot be given

Special predisposing factors
One patient with subacute bacterial endocarditis developed emboli in one lower extremity She was included in this group as she was the only patient with subacute bacterial endocarditis and arterial emboli in the present series 1 patient had cerebral embolism during pregnancy

Autopsy findings
Comparison between clinical and pathologic anatomical diagnoses
Cerebral embolism was found in 12 patients at autopsy All had been clinic ally diagnosed

Emboli in mesenteric arteries were demonstrated at autopsy in 1 case This diagnosis had also been established clinically

Emboli in the splenic artery were found in 4 cases at autopsy In 1 case the clinical diagnosis had been established owing to typical pain below the left costal margin tenderness and a rise of temperature In the other 3 cases the splenic embolism had not been diagnosed as the clinical picture was dominated by pulmonary embolism in 1 case and by emboli in the lower extremities in 2 cases

Recent emboli in renal arteries were found at autopsy of 8 patients In only 1 case had the condition been diagnosed clinically 5 out of the 7 other cases had arterial emboli of different localization at the same time

Cicatrices after previous kidney infarctions were seen in 16 cases Only one had presented characteristic clinical symptoms of renal embolism

In this group cerebral emboli had thus been correctly diagnosed in all cases The same applies to emboli in the mesenteric artery

With regard to emboli in the splenic and renal arteries however the clinical and the pathologic anatomical diagnoses differ The former were correct but at the clinical examination 3 out of 4 splenic infarctions 7 out of 8 recent and 15 out of 16 previous kidney infarctions had been overlooked

These findings with regard to the certainty of the clinical diagnosis of embolism are in accord with statements in the literature (*Daley et al*)

Thrombi in the heart

In 12 out of 17 well described cases with recent or previous arterial emboli autopsy revealed thrombi in the left atrium or in the left auricle The 5 cases showed no focus from which the embolism might have arisen

Prognosis

Recurrence of arterial embolism

Of all 75 patients with arterial emboli 18 (24 per cent) died owing to the first embolic episode These patients are mentioned in detail below

Of the 57 patients who survived the first arterial emboli 28 (48 per cent) later had another episode The number of embolic episodes and the interval between these have been previously mentioned But it may be pointed out here that there is a high incidence of recurrences in patients surviving the first embolic episode

Lethality

Sixty one out of the total series of 75 patients with arterial emboli in the systemic circulation died at an average age of 48 7 years 14 at an average age of 51 3 years survived at the time of the follow up

Death as the direct consequence of arterial emboli occurred in 27 patients 18 died owing to the first embolic episode and 9 as a consequence of recurrences 36 per cent in all of all patients with arterial emboli and 44 per cent of all fatal cases in this group died as a direct consequence of arterial embolism

Nineteen patients died of cerebral emboli i e 25 per cent of the whole series and 31 per cent of all deaths With regard to the 8 other deaths 1 was caused by mesenteric embolism 2 by emboli in the aorta or in its larger visceral branches and 5 by emboli in the extremities with simultaneous abdominal emboli *28 out of the remaining 34 patients died of heart failure (in 9 in conjunction with pulmonary embolism)* 5 died of infections (3 of pneumonia and 2 of sepsis like conditions) and the cause of death was different in 1 case

Survival after first occurrence of arterial emboli

(1) *Deaths*

Nine patients died of recurrent arterial embolism 3 within 1 year after the first episode 2 after 3 years and the last 4 after 5 6 8 and 10 years respectively

Of the 28 patients who died of heart failure 5 died within 1 year after the first embolic episode Then follows a fairly even distribution of the cardiac deaths on the next age groups 10 patients in all died within 3 years 15 within *5 years and 26 in all in the course of 10 years* 2 *patients died of heart failure* after 14 and 18 years respectively

Of the 6 patients who died of causes other than embolism or of infection 5 died in 10 years and the sixth within 11 years after the first embolic episode

(2) *Survivors at the follow up*

Fourteen patients with past arterial embolism survived at the time of the follow up The group includes 8 who had been observed for less than 5 years while 6 survived over 5 years after the first emboli appeared 3 out of the 6 survived more than 10 years after the attack 8 patients had no complaints caused by past arterial embolism 4 out of the 8 had had cerebral emboli including one with emboli in upper and lower extremities as well whereas the *lower extremities had been affected in 4 patients*

Six surviving patients still had hemiparesis after cerebral emboli 2 2 4 7 7 and 10 years ago respectively

Total assessment of the survival after first arterial emboli

As already mentioned 18 out of 75 patients died in the first embolic episode The survival curve shown in Fig 16 has been calculated for the 57 patients surviving the first episode It appears that 55 per cent of these survived 5 years 20 per cent survived 10 years and 6 per cent 16 years

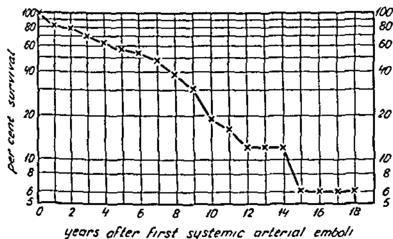


Fig 16

Survival curve of 57 cases of isolated mitral stenosis surviving the first arterial emboli

It may be added that 6 out of 14 survivors presented severe permanent changes after cerebral emboli (hemiplegia)

Patients developing arterial emboli thus had a grave prognosis in the present series

Discussion and Summary

Arterial emboli in the present series developed in patients at comparatively advanced ages (averaging 45 2 years) and at rather advanced stages of the disease 85 per cent of cases in which details were available thus had auricular fibrillation 36 per cent had right heart failure and 13 out of 16 examined roentgenologically had cardio thoracic indices over 54

The age distribution in the present series when the first arterial emboli occurred corresponds exactly to that given in series analysed by *Harris and Levine Lenègre et al* and *Daley et al*

Auricular fibrillation when emboli first occurred in these series of cases was present in 76 per cent 81 5 per cent and 91 per cent in the order mentioned above and right heart failure occurred in the same series in 68 per cent 68 per cent and 34 per cent of cases The present series is in accord with these findings

In cases developing arterial emboli in the present series the prognosis was grave One fourth of all with this complication died when it first developed and over one third of all deaths were due to arterial emboli Correspondingly *Daley et al* found that 12 per cent died of the first attack of embolism and that 41 per cent died of the first or of subsequent attacks

With regard to cerebral emboli alone both *Harris and Levine* and *Lenegre et al* found a direct lethality of 33 per cent In the present series 13 out of 52 patients in all with cerebral emboli died of the first attack (25 per cent) and 19 in all died of the first or of subsequent cerebral emboli (37 per cent) this corresponds to the lethality in the total series of arterial emboli 6 out of 10 who survived cerebral emboli had severe persistent pareses

The average age of patients with arterial emboli was higher than that found in the total series of mitral stenoses both at death and at the follow up

Arterial emboli were thus a serious complication in the course of mitral stenosis in the present series It generally appeared at an advanced age and at rather an advanced stage of the disease The direct lethality was high and the prognosis in cases with a past first attack was grave as only half the patients survived from 6 to 7 years A considerable number of survivors had severe sequelae

PREGNANCY AND THE COURSE OF MITRAL STENOSIS

Pregnancies in the present series

Of the 194 women of the present series 125 (65 per cent) were pregnant once or several times 109 women (56 per cent) gave birth to one or several liveborn children

The 125 pregnant women had had 378 pregnancies in all ending as follows Delivery of liveborn child in 322 cases stillbirth in 10 cases spontaneous abortion in 15 cases induced abortion in 29 cases and death during pregnancy in 2 cases

The number of liveborn children is distributed as follows 30 women gave birth to 1 child 31 to 2 children 15 had 3 children 13 had 4 8 gave birth to 5 children 5 bore 6 children 2 had 7 3 had 8 1 had 12 and 1 had 13 live born children

Pregnancy with delivery of a liveborn child was thus very frequent in the present series

It is therefore natural to mention briefly the more essential events observed during the course of mitral stenosis in connection with pregnancy in the present series

Hearts complaints during pregnancy

With the increasing demands on the function of the heart caused by normal pregnancy it must be expected that the degree of heart trouble may increase during pregnancy in patients with mitral stenosis

Fifty out of 1?ɔ pregnant women (40 per cent) stated that they felt more troubled by their hearts during pregnancy In 10 cases there was an aggravation of heart complaints present in advance and in 10 cases the patients stated that their symptoms had set on during pregnancy

In ?4 out of 50 cases (48 per cent) the heart complaints increased during the first pregnancy In 13 cases the symptoms did not aggravate until during the second pregnancy in ı cases during the third in 4 cases during the fourth in 1 case during the fifth and in 1 case during the seventh pregnancy

In ı5 cases no aggravation of the heart symptoms occurred during pregnancy In 9 of these cases heart symptoms were present in advance whereas 66 did not develop symptoms until after the pregnancies

Nature of heart complaints during pregnancy

In the great majority of patients with increasing complaints during pregnancy the aggravation was in the form of increasing dyspnoea on exertion palpitation premature beats or fatigue

Of special complications during pregnancy mention may be briefly made of the following –

Cardiac asthma or acute pulmonary oedema occurred in 4 patients

(1) A woman aged ?3 suffering from dyspnoea on exertion from the age of years had several attacks of cardiac asthma and acute pulmonary oedema with haemoptysis in the fourth month of pregnancy Delivery at term of a stillborn child Afterwards she had only slight dyspnoea on exertion At the age of 37 the heart disease progressed with development of right heart failure and she died in heart failure at that age

( ) A woman aged 31 She had had uncomplicated deliveries when she was ?1 and ?3 At the age of ?6 she developed heart s mptoms during her third pregnancy In the third month of her fourth pregnan y at the age of 31 she had several attacks of cardiac asthma and acute pulmonary oedema She wanted to go to term and was then feeling well until she suddenly d ed at the age of 37

(3) A woman aged 23 who had had heart compl nts from her 0th year had a slight aggravation during her first pregnancy and aborted in the 6th month A few days later she developed acute pulmonary oedema imp oved somewhat tho gh sh was still exhausted with pronounced dyspnoea on exert on 6 months lat r she had aur cular fibrillation w th cerebral emboli and hemipa e s 14 months after the abort on he died of pneumonia

(4) A woman aged 29 who had had two uncompl cat d deliveries at ages of 21 and ?6 had her third uneventful del very at the age of 29 but developed acute pul monary oedema the next day She then had pronounced dyspno a on exert on but no acute attacks unt l she died at the ag of 34 du ng another att ck of acute pulmonary oed ma

Haemoptysis

Haemoptysis occurred in 3 patients of this group

(1) A woman aged 28 who had had heart symptoms from her 24th year had several haemoptyses at the age of 28 When she was 32 she had several haemoptyses again during the last months of her first pregnancy Chloroform anaesthesia was administered to induce delivery but suddenly she collapsed and died

(2) A woman aged 23 developed heart symptoms and next year during her second pregnancy she had repeated haemoptyses abortion was therefore induced Afterwards the patient had increasing dyspnoea on exertion later also at rest She died in heart failure at the age of 27

(3) A woman aged 44 who had previously had 6 uneventful pregnancies developed persistent heart trouble during her seventh pregnancy at the age of 36 During her eighth pregnancy at the age of 44 she had repeated haemoptyses Pregnancy was carried through and she delivered a liveborn child Afterwards her heart disease was slowly progressing At the age of 67 she died of heart failure

Paroxysmal tachycardia

This occurred in 2 patients during pregnancy One had had previous attacks these were much accentuated during 2 pregnancies with delivery of liveborn children The patient was still alive after 12 years The other patient first had tachycardia during her second pregnancy when she was 35 It recurred only once 13 years later the patient died of pneumonia

Auricular fibrillation and right heart failure

Four patients developed auricular fibrillation right heart failure or both signs during pregnancy or puerperium

(1) A woman aged 23 who had had heart symptoms from her 6th year had an attack of auricular fibrillation in the 9th month of pregnancy She died 3 days after Caesarean section when she was delivered of a liveborn child in an acute attack of rapid auricular fibrillation Autopsy revealed a severe mitral stenosis but no emboli

( ) A woman aged 2? with heart symptoms from her 10th year after delivery of a liveborn child she developed auricular fibrillation during the puerperium Her condition deteriorated constantly with development of right heart failure of which she died within a year

(3) A woman aged 33 with heart symptoms from her 29th year during the 4th month of her first pregnancy she developed auricular fibrillation and right heart failure Following induced abortion in the 6th month her condition remained permanently aggravated 3 years later she died in heart failure

(4) A woman aged 37 with heart symptoms from her 13th year developed right heart failure during the 7th month of her first pregnancy She was delivered of a liveborn child by Caesarean section Right heart failure persisted and during the next year she developed auricular fibrillation The patient was alive 9 years later

In ? cases with *chronic auricular fibrillation* pregnancies were carried through without special complications

Subacute bacterial endocarditis — This was present during the first pregnancy of a woman aged 26 who had had heart symptoms from her 18th year She died one month after delivery of a liveborn child

Cerebral embolism in pregnancy was present in a woman aged 45 who had delivered 5 liveborn children before she developed heart symptoms at the age of 36 during her 6th pregnancy Later induced abortion was performed twice in the third month of her eighth pregnancy when she was 45 she had acute cerebral embolism and died

Deaths or persistent aggravation of heart symptoms in conjunction with pregnancy

Deaths

Two deaths occurred during pregnancy and 2 during puerperium Four in all out of 125 pregnant women died during pregnancy or puerperium (3 per cent)

Of the 2 women who died during pregnancy one died in collapse under chloroform anaesthesia In this case the fatal outcome can hardly be directly attributed to pregnancy The other patient died of cerebral embolism in the third month of pregnancy As death of cerebral embolism is no infrequent occurrence in mitral stenosis in general it is presumably doubtful whether pregnancy can be considered the direct cause of death in this case

Death in the course of the puerperium was caused in one case by acute fatal auricular fibrillation and in the other one by subacute bacterial endocarditis In these cases it is more difficult to evaluate the importance of pregnancy and delivery to the fatal outcome but pregnancy has undoubtedly been at least contributory

The total result is thus that dea h occurred during pregnancy and parturition in the present series in 4 out of 125 patients with mitral stenosis (3 2 per cent)

Bumm and Appel (1950) have collected a total of 28 series of cases from the literature and found an average lethality during pregnancy and puerperium of 3 41 per cent among 6 352 women in all with rheumatic heart disease The analysis chiefly comprised Anglo Saxon series of the period *1936–48*

Persistent aggravation of the heart disease after pregnancy and parturition was stated by 28 patients in all 5 were mentioned above in 1 case the aggravation commenced with acute pulmonary oedema during puerperium in 1 with repeated haemoptysis during pregnancy and in 3 cases with auricular fibrillation or right heart failure during pregnancy In the other cases the aggrava

tion was chiefly in the form of increasing dyspnoea on exertion persisting after the pregnancy

Twenty eight out of 125 pregnant women thus stated that their heart disease had aggravated after pregnancy (23 per cent of all pregnant women)

Since as previously mentioned most patients of this group had had symptoms for some time before the pregnancy and thus risked a spontaneous progression of the disease it is difficult to evaluate to what extent the aggravation was due to the pregnancies and how much spontaneous progression accounts for

Ninety three out of 125 pregnant women stated that the heart disease did not aggravate as a direct consequence of pregnancy or parturition (74 per cent of all pregnant women)

Influence of pregnancy and parturition on the subsequent course of mitral stenosis

As pointed out in *Julius Jensen* s monograph (1938) a real evaluation of the influence of pregnancy on the ordinary course of mitral stenosis is an insoluble task An investigation might be carried through if two comparable series of women with mitral stenosis could be procured one with the other without pregnancies However in all series of mitral stenosis pregnancies will be so frequent that a usable series of non pregnant women to be used for comparison cannot be procured A selection would take place so that the majority of the mildest cases of the disease would consist of pregnant women and the group of non pregnant would show a preponderance of cases with early progression If the latter were left out the remaining group of non pregnant cases would be so small that a comparison would be very doubtful This has been confirmed to the full in the present series and the problem will therefore not be dealt with in detail

Summary

In the present series of isolated mitral stenoses pregnancy and parturition were frequent 125 out of 194 women (65 per cent) had been pregnant once or several times and 109 women (56 per cent) had given birth to one or several liveborn children Induced abortion was performed in 29 cases Death during pregnancy or puerperium occurred in 4 cases (3 2 per cent) Persistent aggravation of the heart disease after pregnancy was stated by about one fourth of the patients who had been pregnant chiefly those who had heart complaints in advance Three fourths of this group had had one or several pregnancies without persistent aggravation of the heart disease these were mostly patients who had had no heart symptoms before An examination of the influence of pregnancies on the ordinary course of the mitral stenosis could not be carried through

ARTERIAL BLOOD PRESSURE IN MITRAL STENOSIS

This section gives a survey of the arterial blood pressure in isolated mitral stenosis.

The arterial blood pressure has been measured in almost all cases of the present series The apparatus used was an aneroid manometer frequently corrected by comparison with a mercury manometer In the case of the hospitalized patients repeated measurements were generally performed at intervals of one or several days In these cases neither the highest nor the lowest but the more stable mean value read was chosen to indicate the patient s arterial blood pressure In the case of outpatients there is generally only one result of measurement fixed after 3 measurements at intervals of a few minutes

Therefore the series is not quite uniform with regard to the procedure used in measuring the blood pressure This however will not be of decisive importance to the ensuing evaluation of the results as an analysis of the cases admitted to the department has shown that there are but slight differences between the blood pressure on the first day and the stable values found later on Considered from the number of patients with an arterial blood pressure over 150/90 mm Hg an evaluation based upon the first measurement would give only 3 per cent more in this group than an evaluation from the most stable value

Arterial blood pressure in the present series

This was measured in 190 women and 76 men of the present series at the first examination and in 55 women and 15 men at the follow up

Arterial blood pressure at the first observation

Fig 17 shows the curves representing the average systolic and diastolic blood pressures in both sexes at the first examination the series is divided into age groups It appears that the average systolic blood pressure in women shows a fairly even rise from about 115–120 mm Hg in patients under 20 to about 140–150 mm Hg in those over 70 years of age Except for the age group 15–49 which had a higher average blood pressure the average systolic blood pressure in males showed essentially the same rise with advancing age

The average diastolic blood pressure shows a similar even though somewhat less pronounced rise from about 65 mm Hg in patients under 20 years to about 75 mm Hg in those over 70

In cases of mitral stenosis *Levine and Fulton* (1928) *Tricot et al* (1951) and *Gray* (1954) have reported exactly similar rises in the average blood pressure with advancing age

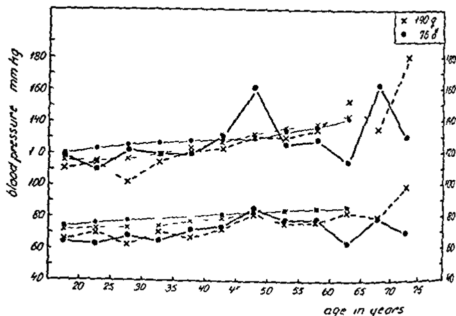


Fig 1ı
The curves show the average systolic and diastolic blood pressures in 5 year groups in the present series Males ●———● and females X X The average curves found by *Master et al* are shown for compari on Males ●———● and females X---X

It is a well known fact that the average systolic and diastolic blood pressu e rises with advancing age in both diseased and healthy individuals The lite rature on thi subject has been reviewed by *Bechgard* (1946) and by *Master et al* (1952) During recent years more extensive investigations of the height of the arterial blood pressure in relation to age in the average population have been undertaken by *Pickering* (1952) *Weiss* (1950) and by *Master et al* (1952) It appears from these publications that the rise in the average systolic and diastolic blood pressure with advancing age is greater than previously supposed *Master et al* (1952) examined the blood pressure in about 15 000 persons who were fit for work and stated that they were in good health On the basis of these examinations the authors calculated the values of the average systolic and diastolic blood pressures with advancing age in women and men These values are reproduced in Fig 17 for the age groups from 16 to 65 years and show a level and a rise with advancing age which in all essentials correspond to the findings in the present series

The average systolic and diastolic blood pressures in the present series of cases of mitral stenosis thus showed exactly the same tendency to rise with advancing age as was found by *Master et al* in a normal population and the rise was of the same order of magnitude

Arterial hypertension in the present series

Hitherto it has most frequently been the usual practice to consider an arterial blood pressure exceeding a certain definite limit e g 150/90 mm Hg as pathologically increased This also appears from the literature on arterial blood pressure in mitral stenosis For the purpose of comparing the present series with the most important findings in the literature the frequency of an arterial blood pressure of 150/90 mm Hg or more in the present series is shown in Table 53 in relation to age

Among women in the present series a total of 38 out of 190 (20 per cent) had an arterial blood pressure of 150/90 mm Hg or more including 10 out of 115 (9 per cent) under 45 years and 28 out of 75 (37 per cent) over 45 years In the case of men the corresponding frequency was 18 in all out of 76 (24 per cent.) namely 7 out of 44 (16 per cent) under 45 years and 11 out of 32 (34 per cent) over 45 years

TABLE 53

Arterial Hypertension in Isolated Mitral Stenosis at First Observation

Females

Ag	N mbe	A t l blood p 150 90 mm Hg m		L m ts d g t M t t l (195) Bl d p		C f p t d g th l m t	
		N mbe		Sy t l	D t l	N mb	
15-19 years	4	–	–	140	90	–	–
20-24	13	–	–	140	90	1	8
25-29	10	–	–	140	92	–	–
30-34	25	2	8	145	95	–	–
35-39	34	6	18	150	98	2	6
40-44	29	2	7	165	100	1	3
45-49	30	10	33	175	105	1	3
50-54	15	4	27	180	108	1	7
55-59	19	7	37	185	108	1	5
60-64	6	4	67	190	110	1	17
65-69	4	2	50	–	–	–	–
70-74	1	1	100	–	–	–	–
Total	190	38	20			8	4
Under 45 years	115	10	9			4	4
Over 45 years	75	28	37			4	5

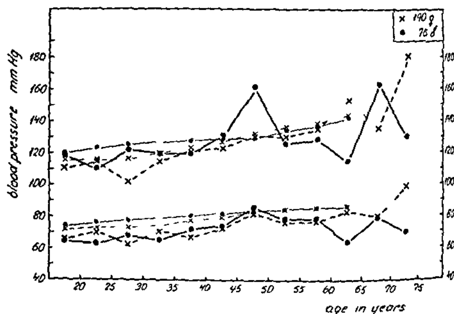


Fig 17

The curves show the average systolic and diastolic blood pressures in 5 year groups in the present series Males •———• and females X X The average curves found by *Master et al* are shown for comparison Males •———• and females X---X

It is a well known fact that the average systolic and diastolic blood pressure rises with advancing age in both diseased and healthy individuals The literature on this subject has been reviewed by *Bechgard* (1946) and by *Master et al* (1952) During recent years more extensive investigations of the height of the arterial blood pressure in relation to age in the average population have been undertaken by *Pickering* (1952) *Weiss* (1950) and by *Master et al* (1947) It appears from these publications that the rise in the average systolic and diastolic blood pressure with advancing age is greater than previously supposed *Master et al* (1952) examined the blood pressure in about 15 000 persons who were fit for work and stated that they were in good health On the basis of these examinations the authors calculated the values of the average systolic and diastolic blood pressures with advancing age in women and men These values are reproduced in Fig 17 for the age groups from 16 to 65 years and show a level and a rise with advancing age which in all essentials correspond to the findings in the present series

The average systolic and diastolic blood pressures in the present series of cases of mitral stenosis thus showed exactly the same tendency to rise with advancing age as was found by *Master et al* in a normal population and the rise was of the same order of magnitude

TABLE 54

Arterial Blood Pressure in Mitral Stenosis Frequency of Arterial Blood Pressure ≥ 150 90 mm Hg

	All ages	Over 45 years	Under 45 years
	%	%*	%**
Boas and Fineberg (1926)	29	53	[illegible]
Levine and Fulton (1928)		58	
Aastrup (1937)		45	
Horns (1944)	24	30	13
Baker and Musgrave (194[illegible])		*30*	
Roseman and Wasserman (1951)	20	32	11
Gray (1954)	17	28	8
Present series of cases —			
Females	20	37	9
Males	24	34	16
Total in present series	21	36	11

* over 40 years ** over 50 years

consider that the middle 95 per cent of all their results of measurement are definitely or probably normal blood pressures whereas the upper 2 5 per cent of all measurements are probably increased (and the lower 2 5 per cent probably low blood pressures)

The limits of the normal blood pressures fixed by *Master et al* are given in Table 53 for each 5 year group together with the number of patients in the present series whose blood pressures exceeded these limits It appears that 8 females (4 per cent of females) and 7 males (9 per cent) had arterial blood pressures exceeding the limits of the normal as stated by *Master et al* 15 in all out of 266 patients (6 per cent) thus had probable or definite arterial hypertension As the American series of normal individuals had 2 5 per cent with blood pressures exceeding these limits it appears that the comparison showed no decidedly higher frequency of hypertension in the present series of cases than in the former

Consequently it seems justifiable to assume that arterial hypertension is not decidedly more frequent in mitral stenosis than in the average population in general

An analysis of the arterial blood pressure measured at the follow up showed similar results and therefore requires no comment

TABLE 53 (continued)
Males

Age	Number	Arterial blood pressure 150/90 mm Hg or more		Limits according to Master et al (19..) Blood pressure		Cases of present series exceeding them	
		Number	%	Systolic	Diastolic	Number	%
15–19 years	3		–	145	90	–	
20–24	5		–	150	95	–	–
25–29	7	–	–	150	96	–	
30–34	10	2	20	155	98	–	–
35–39	11	1	9	160	100	1	9
40–44	8	4	50	165	100	–	–
45–49	9	4	44	170	104	4	44
50–54	10	3	30	175	106	–	–
55–59	8	3	38	180	108	2	25
60–64	2	–	–	190	110	–	–
65–69	2	1	50	–	–	–	
70–74	1	–	–	–	–	–	
Total	76	18	24			7	9
Under 45 years	44		16			5	11
Over 45 years	32	11	34			2	6

In Table 54 the frequency of an arterial blood pressure of 150/90 mm Hg or more in the present series is compared with the frequency of this finding in the most important series of mitral stenosis reported in the literature The table shows that the findings in the present series are in fine accord with those of other authors

Horns (1944) *Roseman and Wasserman* (1951) and *Cray* (1954) all had a series of other categories of patients for comparison and found that the frequency of arterial blood pressure over 150/90 mm Hg in their cases of mitral stenosis did not definitely exceed that in the series used for comparison

No Danish investigations of the distribution of the blood pressure in the average population are available and as it was desired to evaluate the frequency of high blood pressures in the present series it was compared with that of normal individuals collected by *Master et al* On the basis of blood pressure measurements in about 15 000 North American citizens who were fit for work and stated that they were in good health *Master et al* fixed their limits of the arterial blood pressure according to statistical methods They

TABLF 54

Arterial Bl'd Pressure in Mitral Stenosis Frequency of Arterial Blood Pressure ≧ 1 0 90 mm Hg

	All ag	O er 45 ye s	U d 4 y
	%	%	%
Joas and Fineberg (1976)	09	5	7
r me and Fulton (1979)		58	
Lastrup (1937)		48	
r ms (1944)	24	30	13
arer a d Musgrave (1947)		30	
seman and Wasserman (1951)	20	32	11
ray (1954)	17	28	6
resent series of cases –			
males	09	3,	9
ales	24	34	16
tal in present series	21	36	11

' er 40 years * over 50 years

consider tha' the middle 95 per cent of all their results of measurement are definitely or probably normal blood pressures whereas the upper 2 5 per cent of all measurements are probably increased (and the lower 2 5 per cent prob ably low blood pressures)

The limits of the normal blood pressures fixed by *Master et al* are given in Table 53 for each 5 year group together with the number of patients in the present series whose blood pre sures exceeded these limits It appears that 8 females (4 per cent of females) and 7 males (9 per cent) had arterial blood pr s ures exceeding the limits of the normal as stated by *Master et al* 15 in al out of 206 patients (6 per cent) thus had probable or definite arterial hypertension As the American series of normal individuals had 2 5 per cent with blood pressures exceeding these limit it appears that the comparison showed no decidedly higher frequency of hypertension in the present series of cases than in the former

Consequently it *seems justifiable* to assume that arterial hypertension is not decidedly more frequent in mitral stenosis than in the average population in general

An analysis *of the arterial* blood pressure measured at the follow up showed similar results and therefore requ res no c mment

Clinical features

Arterial hypertension was a conspicuous feature in only 3 cases which may be briefly mentioned

(1) *Case report* – A man aged 49 who had had rheumatic fever at the age of 1? and later 1 recurrence developed heart symptoms in the form of dyspnoea when he was 49 He was *admitted with acute* hemiplegia The arterial *blood pressure* was ?10/100 *mm Hg* He had sinus rhythm negative T_1 and T and left axis deviation in the electrocardiogram and the cardio thoracic index was 49 Clinical examination revealed a presystolic murmur at the apex There were no signs of *right* heart failure He died in the department of cerebral haemorrhage *Autopsy showed* mitral stenosis and a large cerebral haemorrhage

(2) *Case report* – A woman aged 48 who had had rheumatic fever at the age of 1? She had a recurrence when she was 2? and developed dyspnoea on exertion at the age of ?3 She was admitted to the department with right heart *failure at the age of 48* Clinical examination revealed a *presystolic apical murmur* The electrocardiogram showed left axis deviation negative T_1 and sinus rhythm The cardio thoracic index was 57 and the left ventricle bulged in exposures in the postero anterior position The arterial blood pressure was 230/130 mm Hg She died in the department of cerebral haemorrhage *Autopsy showed* mitral stenosis and a large cerebral haemorrhage

(3) *Case report* – A woman aged 40 who had had rheumatic fever at the age of 12 Later she had had 5 recurrences and from her 14th year she had suffered from palpitation and dyspnoea on exertion At the first *examination compensation* was satisfactory *Clinical examination revealed* a diastolic *rolling apical murmur* The electrocardiogram showed auricular fibrillation QRS axis +60 – +90 degrees and normal T waves The cardio thoracic index was 51 and she was considered belonging to Class III The arterial blood pressure was 1?0/70 mm Hg At a follow up *7 years later the* blood pressure was 230/110 mm Hg The *electrocardiogram showed left* axis deviation negative T_1 and T *and persistent auricular* fibrillation The *cardio* thoracic index was 64 No definite enlargement of the left ventricle could be demonstrated She had right heart failure and was in Class IV Ophthalmoscopy showed large haemorrhages and exudates in the retinae characterized as fundus *hypertonicus* IV and she *was troubled by pronounced dizziness and headache*

In the other cases the arterial hypertension was no decidedly conspicuous feature during the course of the disease

Summary

In the present series of cases of isolated mitral stenosis the arterial blood pressure showed a rise with advancing age This *corresponded* to the *findings* in other similar series and in control series of the average population 36 per cent in all had an arterial blood pressure *of* 150/90 mm Hg or more this is in accord with the findings in other *similar* eries when the patients ages are considered Compared with the series of normal persons published by *Master et al* the frequency *of* pronounced hypertension in the *present series* was not

decid d'ly higher than would be expected in the case of a mere coincidence of mitral stenosis and essential hypertension Only in a few cases was the arterial hypertension a conspicuous feature of the course of the disease

COMPLICATING DISEASES IN THE COURSE OF ISOLATED MITRAL STENOSIS

Mention may be briefly made of the important complicating diseases ob erved during the course of isolated mitral stenosis in the present series

Carcinoma of the breast was seen in 3 cases In one the complication was he cause of death whereas 2 patients are alive after extirpation of the breast

Carcinoma of the pancreas was the cause of death in 1 case

Cancer metastases to the pelvic bones were the cause of death in 1 case

Fibroma of the uterus with necrosis after roentgen irradiation and ensuing eritonitis were the causes of death in 1 case

Myeloid leukosis was the cause of death in 1 case

Pulmonary tuberculosis caused the patient s death in 1 case

Ileus accounts for 2 deaths

The following non fatal complications occurred —

Psychosis in 2 patients

Severe psychopathy in 1 patient

Disseminated sclerosis in 1 case

Epilepsy in 5 cases

Rheumatoid arthritis in 3 cases

Polyarthrosis in 1 case

Diabetes mellitus in 1 case

Pronounced *exophthalmic goitre* in 1 case

Abdominal tumour of unknown origin in 1 case

These complicating diseases occurred with a frequency which may be con idered a mere coincidence

Finally mention may be made of the incidence of *syphilis* in the present series Only 4 out of 2[illegible]1 patients with isolated mitral stenosis (1 5 per cent of the series) had had syphilis the diagnosis was established from a past history of syphilitic infection or from a positive Wassermann test At autopsy none of these 4 cases presented signs of cardiovascular syphilis Wassermann s test was made in 187 out of the 26[illegible] patients who had had no syphilitic infection the result was negative Syphilis thus played no part in the course of the dis ease in the present series

THE PROGNOSIS OF ISOLATED MITRAL STENOSIS

It appears from the preceding sections that isolated mitral stenosis in th present series showed signs of progression in the great majority of cases Mos patients gradually developed auricular fibrillation and right heart failure A considerable number have had arterial emboli in the systemic or the pulmo nary circulation and a total of 70 per cent of the whole series died durin the period of observation

With regard to the duration of the course of the disease from the early stag with slight symptoms to the terminal stage with absolute heart failure and death there were however considerable variations In some cases the course of the disease was fulminant and the patients died a few years after the onse of the heart symptoms In others the condition remained almost unchanged for a great number of years Nothing in the analysis of the series suggested that it would be possible to estimate with certainty in what cases the course would be rapid and malignant and in what cases a more benign course migh be expected

The following of the most important results of the survival analyses previ ously performed may be briefly recapitulated –

The age at the initial rheumatic infection the number of rheumatic recur rences or the age when the first heart symptoms set on afforded no safe guidance with regard to the subsequent course

In most cases auricular fibrillation was a rather late sign during the course of the disease and only about one third of the patients survived more than 10 years after it has been ascertained

Right heart failure was a late sign during the course of mitral stenosis Half the patients survived 2 or 3 years and only about one tenth survived 10 years after it had been ascertained

Cardiac asthma and acute pulmonary oedema were rare symptoms in the present series and seldom causes of death Of patients surviving the first attack about two fifths survived more than 10 years

Isolated haemoptysis was also comparatively rare in the present series and was not the cause of death About half the patients with this symptom survived 10 years after the first haemoptysis

Pulmonary infarctions chiefly occurred at more advanced stages of the dis ease most frequently in patients with right heart failure and auricular fibril lation Two fifths of the patients died immediately after the development of the first pulmonary infarction and one fifth of the rest survived more than 10 years

Arterial emboli in the systemic circulation also constituted a late symptom in the course of the disease and frequently occurred in patients with auricular fibrillation and rather often simultaneously with right heart failure One

fourth of the patients died in the first attack and about one fourth of the rest survived more than 10 years

The survival times found after the most important complications in mitral stenosis may afford some guidance in estimating the prognosis of the disease but there is a large group of cases in which it cannot be assessed solely from these experiences

To attempt a more thorough evaluation of the prognosis the survival in the series will be examined in the following with the *condition at the first observation* as the starting point

Survival after the first observation

a) Material and method

In estimating the survival after the first observation the indirect method of calculation of survival times described on pages 45 to 48 was used here as well as in the preceding sections The survival curves referring to the present series were compared with those applying to the average Danish population on the lines mentioned on page 47

The series of patients comprises the whole of the original series with a few corrections 5 patients have been left out as they died during the first year of the period of observation of diseases (or accidents) with no relation to the mitral stenosis Further 10 patients who died later of diseases without relation to the mitral stenosis have been included among the living patients until the year of death

The series then comprises 266 cases

The corrections were made in order that the calculation of the survival times might be based solely upon the heart disease and its usual complications

b) Survival in the whole series

The survival in the whole series was calculated for females and males separately The survival curve for 192 females at an average age of 41 4 years at the first observation *is shown in the* upper half of Fig 18 It shows a somewhat greater fall during the first year and then a fairly gradual fall during the next 19 years of observation After 10 years 40 per cent survived after 20 years 18 per cent At the top of the same figure the survival curve for 41 year old *women in the average* Danish population of the same period is plotted It appears immediately *that the series* of cases of mitral stenosis shows a very great excess lethality

The survival curve for the whole of the male series is shown in the lower half of Fig 18 The series *comprised* 74 males at an average age of 41 1 years As in the case *of females* the survival curve shows a somewhat steeper fall

during the first year of the period of observation followed by a fairly even fall until the 12th year of observation The course of the curve is then more irregular owing to the comparatively small number of cases left 29 per cent of the whole group survived after 10 years and 8 per cent after 18 years A comparison with the survival curve for 41 year old males in the average Danish population of the same period immediately shows the high excess lethality among cases of mitral stenosis

Both females and males of the present series thus showed a very high excess lethality when compared with the average Danish population

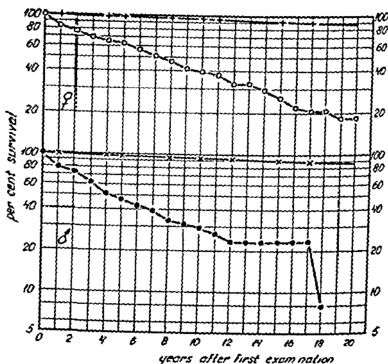


Fig 18

Survival curves in cases of isolated mitral stenosis calculated from the first observation In the upper half the survival curve for 197 females in the lower half for 74 males. Survival curves for corresponding age groups in the Danish population are shown at the top of both diagrams

Fig 18 further shows that males had a lower survival percentage during the period of observation than females Either sex will be considered separately in the following

The groups comprise all degrees of the disease and all age groups To get a better idea of the course of the disease the influence of these factors will be analysed in greater detail in the following

3) Surv al in relation to age at the first observation

The relation of age to the survival in the period of observation was exam ned by dividing the series into 3 groups as shown in Table 55 (1) All pa ents under 36 years (2) all between 36 and 49 and (3) all over 50 years f a e.

TABLE 55

Age and Sex Incidence in the Series

Age gr ps	14 35 y a	36–49 y	50 ye rs m	T l
emales (number)	65	81	46	192
ales	27	2	2	4

In the case of females the survival curves of the three age groups are shown Fig 19 which also gives the survival curves for females at similar average es in the average population Of 65 females under 36 years 39 per cent rvived after 10 years and 25 per cent after 20 years Of 81 females between and 49 years 40 per cent survived after 10 years and 14 per cent after years Of 46 females over 50 years 29 per cent survived after 10 years d less than 10 per cent after 13 years All survival curves show a fairly even ll throughout the period of observation and in comparison with the survival rves plotted for similar groups in the average population all age groups in e series show a high excess lethality

In the case of males similar survival curves are shown in Fig 20 and com ared with the survival curves for males at corresponding average ages in the average population Of 27 males under 36 years 33 per cent survived after 10 years and 17 per cent after 17 years the period of observation being no longer Of 25 males between 35 and 49 years 39 per cent survived after 10 years and 0 per cent after 18 years Of 22 males over 50 years 11 per cent survived after 9 years this being the end of the period of observation in this group The survival curves of these groups follow a somewhat more irregular course as this series was smaller however all groups show a high excess l tha lity in comparison with corresponding groups in the average population

Summing up it can be said that the survival curves for females and males divided into age groups show a greater fall in the survival percentage with advancing age in most cases the age group over 50 in either sex showing the lowest survival percentage This was actually to be expected both because the survival curves for the average population show similar conditions and be cause the older age groups would be expected to contain a relatively higher proportion of more advanced cases of mitral stenosis

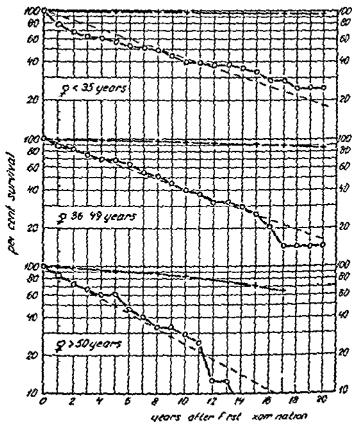


Fig 19
Survival curves for females with isolated mitral stenosis in 3 age groups At the top of each diagram the survival curves for corresponding age groups of females in the Danish population

However as there is such a great difference between the survival curves of the average population and those found in cases of mitral stenosis it must be justifiable to conclude that factors in the disease other than age in itself must be of greater importance to the survival Therefore in the following the patients ages will not be considered but it will first be examined what other factors we may use as indicators of the survival after which the validity of the conclusions drawn will be examined in relation to age

The survival curves in Figures 19 and 20 also show a mean curve from which the average annual probability of death can be determined for the whole series in the period concerned The average annual probability of death means the number of deaths during the period of observation divided by the number of years of observation for dead and living patients in the group It appears that the calculated mean curve corresponds approximately to the survival curve

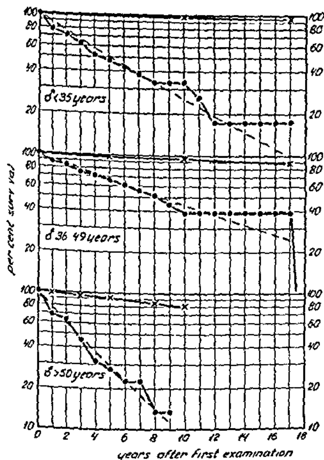


Fig 20
Survival curves for males with isolated mitral stenosis in 3 age groups At the top of each diagram the survival curves for corresponding age groups of males in the Danish population

ld nd The conformity was so good that it was decided for practical reasons to use the average annual probability of death in the following as the basis of a further analysis of the factors examined in relation to the survival

As a help in interpreting the values of the average annual probability of death used in the following sections Table 55 A shows for different values of the average annual probability of death the corresponding survival times in years for 75 per cent survivors for 50 per cent and for 25 per cent respectively

In the following analysis of the survival an average annual probability of death of 0 100 thus means that 75 per cent of the original series survived

TABLE 5 A

Average Annual Probability of Death and corresponding Survival Times

Average annual probability of death	Survival times (years)		
	75 per cent or [illegible]	50 per cent [illegible]	[illegible] per cent survivors [illegible]
0 015	19 0	45	–
0 030	9 4	22 [illegible]	–
0 045	6 2	15 0	30 0
0 060	4 6	11 2	[illegible]4
0 070	3 9	9 6	19 [illegible]
0 080	3 4	8 3	16 5
0 090	3 0	7 4	14 7
0 100	2 7	6 6	13 1
0 110	2 5	6 0	11 9
0 120	[illegible] 3	5 4	10 9
0 130	[illegible] 1	5 0	10 0
0 140	1 8	4 6	9 [illegible]
0 150	1 8	4 3	8 5
0 160	1 7	4 0	8 0
0 170	1 6	3 7	7 5
0 180	1 5	3 5	7 0
0 200	1 3	3 1	6 3
0 300	0 8	[illegible]0	4 0
0 500	0 4	1 0	[illegible]0
1 000	<1	<1	<1

after 2 7 years 50 per cent survived after 6 6 years and 25 per cent survived after 13 1 years (Table 55 A)

The procedure was as follows In the total series of females and males the dependence of the average annual probability of death on the three clinical criteria which are considered the most important in estimating the prognosis was examined These were the size of the heart the heart rhythm and the degree of physical activity These will first be considered separately and then in mutual relationship Conclusions are drawn with regard to the best prognostic division of the series after which the dependence of the division found on the ages of the patients will be examined Finally it is attempted to assess the importance of other clinical criteria to the prognosis

(4) *Dependence of survival on the heart size*

As previously mentioned the classification of the series according to the size of the heart is based on determination of the cardio thoracic index In

In out of 766 cases included in this prognostic study the index was determined by the writer after measurement of the transverse diameter of the heart and of the width of the thorax at the level of the right vault of the diaphragm To obtain a complete assessment of the prognosis the remaining cases have been placed in one of the four index groups This applies to 8 cases in which the roentgenograms had been lost they were grouped according to the description given by the Roentgenologic Department further to 7 cases grouped solely on the basis of the clinical description of the position of the apex beat and to 5 cases grouped according to the clinical description and subsequent autopsy findings The whole series can then be grouped as shown in Table 56

TABLE 56

Heart Size and Probability of Death

Heart size according to cardio-thoracic index	Total number of patients	Deaths during period of observation	Years of life attained	Average probability of death
		Females		
Under 51	37	9	314	0 079
51 54	35	24	309	0 078
55-64	85	59	427	0 138
65 or more	40	33	16	0 198
		Males		
Under 51	18	9	108	0 083
51-54	17	11	101	0 109
55-64	31	23	124	0 185
65 or more	8	8	12	0 667

The series was divided into the following 4 groups according to the cardio thoracic index (1) Index up to 50 (2) index from 51 to 54 (3) index from 55 to 64 and (4) index over 64 The table shows the sex incidence in these four groups the number of patients when the investigation commenced deaths during the period of observation and the number of years of life attained for all patients in the group the last column gives the average annual probability of death

In the case of females there is a distinct rise in the annual probability of death with increasing cardio thoracic index from 0 079 with indices under 51 to 0 078 0 138 and 0 198 in the case of the largest hearts

In the case of males the table shows a similar rise in the annual probabilit of death from 0 083 with indices under ₋51 to 0 109 0 185 and 0 667 in th case of the largest hearts

The tendency is thus that increasing size of the heart results in rising annua probability of death

Furthermore it appears that the annual probability of death is greater males than in females in groups with the same cardio thoracic indices

(5) *Importance of heart rhythm to survival*

The relation of the heart rhythm to survival expressed by the annual prob ability of death is shown in Table 57

TABI F 57

Heart Rhythm and Probability of Death

Rhythm	T t l umbe f p t t	D ath d ng p d 1 6 t n	Y of l f tt d	A erag u l pr b bl ty of d th
		Females		
Sinus rhythm	86	47	708	0 066
Auricular fibrillation	106	77	504	0 153
		Males		
Sinus rhythm	27	16	143	0 112
Auricular fibrillation	47	53	202	0 173

It appears that auricular fibrillation gave a distinctly higher annual prob ability of death than did sinus rhythm In females it was 0 066 in the case of sinus rhythm and 0 153 with auricular fibrillation In males it was 0 112 and 0 173 respectively

(6) *Dependence of survival on the degree of physical activity*

As previously mentioned the series was classified according to the degree of physical activity on the basis of the data available from the first observation and in accord with the table recommended by the American Heart Association The classification and its relation to the subsequent course of the disease are given in Table 58

TABLE 58

Dependence of Survival on Degree of Physical Activity at the First Observation.

Degree of physical activity	Number of patients at first observation	Deaths during period of observation	Years of life [illegible]	Average annual probability of death
Females				
Class II	40	11	436	0 025
Class III	116	77	724	0 106
Class IV	36	3[illegible]	52	0 692
Males				
Class II	17	5	145	0 034
Class III	41	30	183	0 164
Class IV	16	16	17	0 941

It appears that there is a distinct relation between the degree of physical activity at the first observation and the annual probability of death In the case of females the latter thus rose from 0 025 in Class II to 0 106 in Class III and to 0 692 in Class IV In males the corresponding rises were from 0 031 in Class II to 0 164 in Class III and to 0 941 in Class IV

(7) *Survival in relation to degree of physical activity heart rhythm and heart size*

It appears from the preceding analyses that the classification according to the degree of physical activity gave the most distinct differences in the average annual probability of death

It would now be of great interest to examine whether a classification according to heart rhythm and heart size might contribute further to elucidating the average prognosis in the separate classes

Table 13 on page 64 gives the relationship between the three criteria employed Degree of physical activity heart rhythm and heart size It appears that patients in Class II have a high incidence of sinus rhythm and of lower degrees of cardio thoracic index that patients in Class IV most frequently present auricular fibrillation and higher degrees of cardio thoracic index those in Class III show a more even distribution between sinus rhythm and auricular fibrillation on the one hand and all degrees of heart size on the other hand

The three classes will be analysed separately in the following

TABLE 59

Class IV Heart Rhythm Heart Si c and Probability of Death

	Tot l	S u rhythm	Au cul r f b li t
Males			
Cardio thoracic index			
under 51	–	–	–
51–54	1	–	1
55–64	9	4	5
65 or more	6	–	6
Total	16	4	12
Probability of death			
under 51	–	–	–
51–54	1/6 = 0 167	–	1/6 = 0 167
55–64	9 8 = 1 125	4/1 = 4 000	5/7 = 0 714
65 or more	6/3 = [illegible] 000		6/3 = 2 000
Total	16/17 = 0 941	4/1 = 4 000	12/16 = 0 750
Females			
Cardio thoracic index			
under 51	1	–	1
51–54	–	–	–
55–64	15	3	12
65 or more	[illegible]0	3	17
Total	36	6	30
Probability of death			
under 51	1/0 = ∞	–	1/0 = ∞
51–54	–	–	–
55–64	15/14 = 1 071	3/4 = 0 [illegible]50	12/10 = 1 200
65 or more	[illegible]0/38 = 0 5[illegible]6	3/0 =	17/38 = 0 447
Total	36/5[illegible] = 0 692	6/4 = 1 500	30/48 = 0 625

The table describes males and females separately The upper half of each part gives the number of patients in the various groups In the lower half the numerator in the fraction states the number of deaths during the period of observation the denominator stands for the years of life attained of dead and living patients and the result shows the annual probability of death

The distribution of the patients in Class IV is shown at the top of Table 9 with regard to heart rhythm and heart size the average probability of death in relation to these factors is given below

It appears that the average annual probability of death in the whole of Class IV is exceedingly high 0 692 in females and 0 911 in males When the group is divided according to heart rhythm it appears that there is a distinct tendency to a higher annual probability of death in the case of sinus rhythm than in auricular fibrillation in both males and females In sinus rhythm the annual probability of death is 4 000 in males and 1 500 in females In auricular fibrillation the values are 0 750 for males and 0 625 for females With regard to the heart size it appears that almost all patients have been placed in the two uppermost groups and no definite tendencies with regard to the probability of death in these groups can be traced

The tendencies to differences in the annual probability of death according to heart rhythm are of no great practical importance as the prognosis in Class IV is exceedingly poor

With regard to Class III (Table 60) it appears in the case of females that when the group is divided according to heart rhythm there is the same annual probability of death in sinus rhythm and in auricular fibrillation 0 104 and 0 109 respectively In the case of males the corresponding figures are 0 167 and 0 167 respectively A more thorough division of Class III according to heart rhythm thus proved to be non contributory

With regard to the size of the heart the four groups from the lowest to the highest cardio thoracic index had the following probabilities of death in the case of females 0 079 0 108 0 115 and 0 105 and the corresponding figures in the case of males were 0 164 0 133 0 184 and 0 222 Thus there were no differences of importance between the four degrees of heart size in the whole of Class III either in males or in females A further division also considering the heart rhythm suggested no definite tendencies

It can therefore be concluded that no definite advantage can be obtained in Class III by using the heart rhythm or the heart size as subdivisions

It appears from Table 61 that Class II showed a distinct tendency to a greater annual probability of death in the case of auricular fibrillation than in the case of sinus rhythm In females the probability of death in auricular fibrillation was 0 072 as compared to 0 031 in sinus rhythm In males the corresponding figures were 0 058 and 0 013 respectively These differences are so great that the annual probability of death in auricular fibrillation in females is distinctly closer to the same quantity in Class III than to the probability of death in sinus rhythm in Class II In the case of males with auricular fibrillation in Class II the annual probability of death is also somewhat closer

TABLE 60

Class III Heart Rhythm Heart S[illegible]e and Probability of Death

	Total	S[illegible]s [illegible]hythm	Auric[illegible] [illegible]brill[illegible]
Males			
Cardio thoracic index			
under 51	11	8	3
51–54	11	4	7
55–64	17	3	14
65 or more	2	–	[illegible]
Total	41	15	[illegible]6
Probability of death			
under 51	8/49 = 0 163	6/41 = 0 145	2/8 = 0 145
51–54	8/60 = 0 133	4/14 = 0 [illegible]86	4/46 = 0 087
55–64	12/65 = 0 184	1/11 = 0 091	11/54 = 0 [illegible]04
65 or more	2/9 = 0 222	–	[illegible]/9 = 0 [illegible]
Total	30/183 = 0 164	11/[illegible]6 = 0 16[illegible]	19/117 = 0 16[illegible]
Females			
Cardio thoracic index			
under 51	16	14	[illegible]
51–54	26	18	8
55–64	57	15	4[illegible]
65 or more	17	3	14
Total	116	[illegible]0	66
Probability of death			
under 51	8/101 = 0 079	[illegible]/94 = 0 074	1/7 = 0 143
51–54	21/195 = 0 108	16/15[illegible] = 0 105	5/43 = 0 117
55–64	3[illegible]/323 = 0 11[illegible]	10/[illegible]9 = 0 1[illegible]	27/[illegible]44 = 0 111
65 or more	11/105 = 0 105	[illegible]/12 = 0 167	9/93 = 0 097
Total	77/724 = 0 106	[illegible]5/337 = 0 104	4[illegible] 387 = 0 109

The table describes males and females separately The upper half of each part gives the number of patients in the various groups In the lower half the numerator in the fraction states the number of deaths during the period of observation the denominator stands for the years of life attained of dead and living patients and the result shows the annual probability of death

to the same quantity in Class III than to the probability of death in sinus rhythm in Class II

With regard to the calculations of survival it must therefore be considered most appropriate to distinguish between the patients with sinus rhythm and those with auricular fibrillation in Class II

Considering now the influence of the heart size on the annual probability of death in Class II it appears that among the groups with sinus rhythm it is only the females who have several groups of heart size and that there is a slight tendency to a rise with increasing heart size from an annual probability of death of 0 with a cardio thoracic index under 50 to 0 026 with indices from 51 to 54 and to 0 041 with indices from 55 to 64 As this tendency was not found among males the heart size was left out of consideration in this group In the groups with auricular fibrillation in Class II the figures are small and the tendencies doubtful Auricular fibrillation was almost always associated with a cardio thoracic index over 51

In order to make sure that the tendencies found in the annual probability of death might not only depend on a skewness in the age distribution of the series in the separate subdivisions the complete analysis was undertaken solely in cases under 50 years It appeared that all the tendencies found recurred in this analysis

Summing up the analysis of the relation of survival to degree of physical activity heart rhythm and heart size thus showed that the classification according to the degree of physical activity appeared to be the best sole indicator of the prognosis When the class division is combined with one according to heart rhythm it appears that additional classification according to heart size does not afford further information of very great value

As a result of the analyses of survival in the present series four groups have been established these may be briefly mentioned with reference to the basis of classification age and survival in the period of observation

Group A – This comprises patients in Class II with sinus rhythm The group contains 30 female patients at an average age of 34 6 years and with an average duration of symptoms of 9 9 years The survival curve of this group is given in Fig 21 and shows a survival of 85 per cent after 10 years and 70 per cent after 20 years The group contains 8 males at an average age of 36 0 years and with average duration of symptoms of 4 0 years The survival curve of this group is given in Fig 22 and shows a survival of 88 per cent after 10 years and after 17 years This group thus survives many years Of 30 surviving patients in this group a total of 18 (or 60 per cent) showed

TABLE 61

Class II Heart Rhythm Heart Si e and Probability of Death

	T t l	S u rhythm	A ul r f brillat
Males			
Cardio thoracic index			
under 51	7	7	–
51–54	5	1	4
55–64	5	–	5
65 or more	–	–	–
Total	17	8	9
Probability of death			
under 51	1/59 = 0 017	1/59 = 0 017	–
51–54	2/35 = 0 057	0/17 = 0	2/18 = 0 111
55–64	2/51 = 0 039	–	2/51 = 0 039
65 or more	–	–	–
Total	5/145 = 0 037	1/76 = 0 013	4/69 = 0 058
Females			
Cardio thoracic index			
under 51	15	14	1
51–54	9	9	–
55–64	13	6	7
65 or more	3	1	2
Total	40	30	10
Probability of death			
under 51	0/213 = 0	0/196 = 0	0/17 = 0
51–54	3/114 = 0 026	3/114 = 0 026	–
55–64	7/90 = 0 078	2/49 = 0 041	5/41 = 01 [illegible]
65 or more	1/19 = 0 053	1/8 = 0 125	0/11 = 0
Total	11/436 = 0 025	6/367 = 0 016	5/69 = 0 072

The table describes males and females separately The upper half of each part gives the number of patients in the various groups In the lower half the numerator in the fraction states the number of deaths during the period of observation the denominator stands for the years of life of dead and living patients and the result shows the annual probability of death

evidence of progression of the heart disease at the follow up whereas the condition had remained unchanged in 12 cases (or 40 per cent)

Group B – This comprises patients in Class III with sinus rhythm It contains 50 female patients at an average age of 36 5 years and with an average duration of symptoms of 8 5 years The survival curve of this group is given in Fig 21 and shows a survival of 44 per cent after 10 years and 16 per cent after 16 years (then falling below 5 per cent during the next year) There are 35 male patients at an average age of 34 5 years and with an average duration of symptoms of 7 6 years Fig 22 gives the survival curve of this group showing a survival of 13 per cent after 10 years (after the 11th year the survival falls below 5 per cent)

According to the survival curve the median survival time for females of this group is from 7 to 8 years for males from 5 to 6 years

Of 15 survivors in this group a total of 9 (or 60 per cent) showed evidence of progression of the heart disease at the follow up whereas the condition had remained unchanged in 6 patients (or 40 per cent)

Group C – This group comprises patients with auricular fibrillation in Classes II and III It contains 76 female patients at an average age of 45 9 years and with an average duration of symptoms of 11 1 years The survival curve of this group is given in Fig 21 and shows a survival of 46 per cent after 10 years and 11 per cent after 17 years The group contains 35 males at an average age of 42 8 years and with an average duration of symptoms of

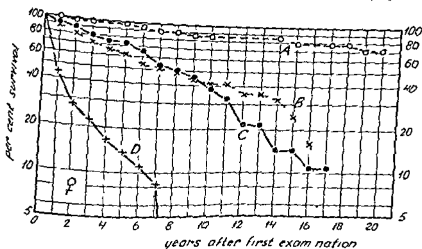


Fig 21
Survival curves for females in the prognosis groups A B C and D

9 3 years Their survival curve is given in Fig 22 and shows a survival o
28 per cent after 10 years falling to 0 per cent after 17 years

According to the survival curve the median survival time for females of this group is from 7 to 8 years for males from 5 to 6 years

Of 37 survivors in this group a total of 22 (or 60 per cent) showed evidence of progression of the heart disease at the follow up whereas the condition had remained unchanged in 15 patients (or 40 per cent)

Broadly speaking this group thus has the same survival times as Group B even though the patients of Group C are about 6–10 years older on the average

Group D – This group comprises patients in Class IV It contains 36 female patients at an average age of 44 1 years and with an average duration of symptoms of 15 1 years Their survival curve is given in Fig 21 and shows a survival of 44 per cent after 1 year 14 per cent after 5 years and falling below 5 per cent after 7 years The group contains 16 male patients at an average age of 45 1 years and with an average duration of symptoms of 12 9 years After 1 year the survival curve of this group fell to 38 per cent after 4 years to 6 per cent and after 6 years to 0 per cent

The median survival time of this group is under 1 year in either sex

Grant's series of ex servicemen mentioned on page 23 lends considerable support to the division into prognostic groups in the present series.

He divided his series according to exercise tolerance" based on exercise tests His classification comprises four degrees which can be equalled approxi

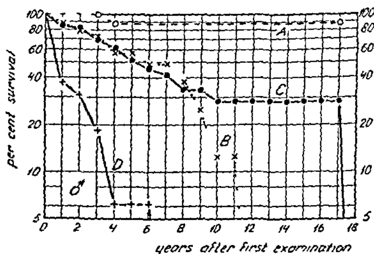


Fig 22
Survival curves for males in the prognosis groups A B C and D

..ly to the four classes recommended by the American Heart Association and used in the present series If the groups good and fair exercise tolerance with sinus rhythm shown in Grant's Table XXXIII are joined it appears that 71 out of 87 patients survived after 10 years (82 per cent) Correspondingly main group A in the present series showed a 10 year survival of .. per cent. of females and 88 per cent of males

Grant's group poor tolerance with sinus rhythm had a 10 year survival of .. per cent. (49 out of 95 patients survived) Correspondingly main group B in the present series showed a 10 year survival of 44 per cent of females and .. per cent. of males

The group termed poor tolerance with auricular fibrillation in Grant's series had a 10 year survival of 47 per cent (16 out of 34 patients survived) In main group C of the present series the survival after 10 years was 46 per cent of females and 28 per cent of males

In Grant's group congestive failure all patients died in 10 years Main group D of the present series showed similar findings

When his series is divided according to the principles used in dividing the present one exactly the same tendencies are found with regard to survival in the two series

The fact that the survival rate in the intermediate groups in Grant's series is somewhat higher is undoubtedly due to his patients being 10 years younger than those in the present series Furthermore his series which as already mentioned, consisted of ex servicemen will naturally comprise fewer cases which become severe at an early stage than the present series

(8) *Influence of other factors on survival*

It was decided to examine from the afore mentioned division into prognostic main groups whether clinical criteria other than those hitherto considered in the analysis of survival might contribute to a safer estimate of the prognosis of the various main groups

The analysis was performed by determining the average annual probability of death in the group with the finding concerned and this result was compared with the annual probability of death in the rest of the main group

The experiences thus gained may be briefly mentioned The analysis was of special interest in main groups A B and C whereas main group D is not considered here as its prognosis was so poor that further analysis was considered of no interest

The influence of *cardiac asthma acute pulmonary oedema and of isolated haemoptysis* was examined as a whole In main group A there was only 1 case among females and 1 among males the analysis was therefore omitted In

main group B these symptoms occurred in 15 out of 50 females the anm probability of death for patients with these symptoms was 0 124 as compar to 0 097 for patients without In males of main group B the symptoms occurr in 8 out of 16 and the annual probability of death for patients with the sym toms was 0 146 as compared to 0 200 for those without This group thus c not show definite tendencies to a poorer prognosis in cases with acute p monary oedema or haemoptyses than in the rest of the group

In main group C acute pulmonary oedema and haemoptyses occurred in out of 76 females and the probability of death in patients with these sympto was 0 088 as compared to 0 107 in the rest of the cases The symptoms occurr in 6 out of 35 males in this main group the probability of death among p tients with the symptoms was 0 286 as compared to 0 103 among those witho This main group thus showed no definite tendencies to a poorer prognosis cases with acute pulmonary oedema and haemoptysis than in cases without

Nothing in the present series thus suggested that cardiac asthma or acu pulmonary oedema or haemoptysis gave an average prognosis in the vario main groups which was poorer than that found in the rest of the main grou

Similar analyses were made in the case of patients with past pulmonary i farction and with past arterial embolism in the systemic circulation but the did not show distinct tendencies to a poorer prognosis for patients with the complications than for the rest of the main group

Electrocardiographic changes

The QRS axis

The significance of a QRS axis to the right of +90 degrees was examine patients with this finding being tested in comparison with the other patien in the separate main groups

In main group A 3 cases of right axis deviation occurred in 30 females ar 1 case in 8 males owing to the small number of positive findings the analys was omitted here

In main group B right axis deviation occurred in 17 out of 30 females th annual probability of death was 0 198 in right axis deviation as compared t 0 074 in the absence of this finding 4 out of 15 males had right axis deviatio and the probability of death was 0 333 as compared to 0 140 in the absence o right axis deviation

Main group B thus showed a uniform tendency to a higher annual probabilit of death in the case of right axis deviation than in the absence of this finding

Main group C showed right axis deviation in 18 out of 76 females and th probability of death was 0 101 as compared to 0 103 in the absence of ri h axis deviation 10 out of 35 males had right axis deviation here the probabilit of death was 0 200 as compared to 0 117 in the rest of the group The male

of this group thus showed the same tendency as those in main group B this was not seen among the females though there was no tendency in the opposite direction.

Summing up it can be ascertained that right axis deviation in main group B gave a tendency to a prognosis that was poorer than that seen in the absence of this sign, whereas the tendency was not so conspicuous in main group C

T wave changes

The relation of the T wave changes to the classification according to physical activity was shown in Table 23 (page 80) It appeared that patients in Class II with sinus rhythm most frequently had normal T waves and more rarely a negative T_3 whereas other T wave anomalies hardly occurred in this group A similar distribution applied to patients in Class III with sinus rhythm as this also comprised a few with $T_1 = 0$ Patients in Classes II and III with auricular fibrillation (regardless of any treatment with digitalis) showed a more even distribution on *normal* T waves negative T_3 and iso electric T_1 In Class IV the great majority of patients had abnormal T waves

Broadly speaking the distribution of the T wave changes thus corresponds to the classification according to physical activity An evaluation of their prognostic importance apart from the prognostic classification of the patients in the main group is difficult For the number of patients with certain definite T wave changes will in rather few cases only be sufficiently large for a comparison with other T wave changes within the same group

Negative T_3 – In main group A 6 females had a negative T_3 with a probability of death of 0 044 as compared to 0 014 in 22 cases with normal T waves There was only 1 case with a negative T_3 among the males for which reason no estimate could be made

In main group B 11 females had a negative T_3 with a probability of death of 0 118 as compared to 0 088 for 31 females with normal T waves Only males had a negative T_3 in this group therefore no calculation was made

In main group C 13 females had a negative T_3 with a probability of death of 0 119 as compared to 0 074 for 32 females with normal T waves Among the males 10 had a negative T with a probability of death of 0 219 as compared to 0 164 for 1 males with normal T waves

There was thus a uniform tendency for patients with a negative T_3 in the groups with a reasonable number with this T wave anomaly to show a similar uniform tendency to a poorer prognosis than that of patients with normal T waves

Negative T_2 and T_3 – This anomaly was present in so few cases that no comparison could be carried through in the present series

Iso electric T_1 with or without other T wave anomalies

Main group A contained so few cases of this nature that the comparison w
not undertaken

In main group B 6 females had an iso electric T_1 with an annual probabil
of death of 0 171 as compared to 0 088 for 31 with normal T waves

In main group C 30 females had an iso electric T_1 with a probability
death of 0 137 as compared to 0 074 for 32 with normal T waves In 5 mal
with an iso electric T_1 the probability of death was 0 160 as compared to 0 0
for 19 males with normal T waves

There was thus a uniform tendency for patients with iso electric T_1 to ha
a poorer prognosis than those with normal T waves within the same ma
group

Generally it can be concluded that the electrocardiographic findings of rig
axis deviation in main Group B of negative T_3 and of iso electric T_1 in mai
Groups B and C indicate that the prognosis is poorer than in the absence
these signs

Chapter V

Clinically Probable Mitral Stenosis

In the present study the criterion for the clinical diagnosis of mitral stenosis was the presence of a characteristic diastolic and/or presystolic apical murmur. It was mentioned in the sections on the diagnostic criteria in the present series of cases of mitral stenosis that the characteristic murmur(s) may subside or be very difficult to hear during phases of the disease with a rapid arrhythmic action of the heart and pronounced heart failure. It is also well known that the diagnosis of mitral stenosis may fail to be established if the patient has been examined only during this stage. This has been pointed out by *Cabot* (1913), *Lewis* (1913), *Warburg* (1913), *Aastrup* (1937), *White* (1946), and was recently stressed again by *Levine and Loze* (1952), who published a small series demonstrating this experience.

In going over the case records of Medical Department B, the University Hospital, Copenhagen, the clinically safe cases of mitral stenosis were sorted out. This left a smaller group of cases which had been clinically suspected of mitral stenosis but lacked the characteristic murmur. Mitral stenosis was later verified at autopsy in 6 of these cases, and they were included in the series of unquestionable cases. This left 21 patients in whom mitral stenosis could not be verified later, as they were not autopsied after their death. This group may be briefly mentioned here.

The group "clinically probable mitral stenosis" includes cases which had presented several of the secondary signs or symptoms usually constituting part of the clinical picture in isolated mitral stenosis. Mention may be made here of these signs: A past history of rheumatic infection, auricular fibrillation, systolic murmur or an accentuated first sound at the apex, mitral snap, right axis deviation in the electrocardiogram, roentgenologic enlargement of the left atrium or straight left contour of the heart with possible bulging of the second left arch, and a past history of arterial embolism.

The following is a brief survey of the series with special reference to the clinical course.

Cases of probable mitral stenosis at the first observation

The series comprised 21 patients, 9 males and 12 females. The age distribution and the most important findings at the first observation are given in Table 62.

TABLE 62

Cases of Probable Mitral Stenosis at the First Observation

	20–29	30–39	40–49	50–59 years	Total
Males	1	1	5	2	9
Females	1	–	7	2	12
Total	2	3	12	4	21
Auricular fibrillation	–	3	12	3	18
Right heart failure	–	3	5	2	10

Sixteen out of the 21 patients were over 40 years of age at the first observation and 4 were over 50 years The average age at the first examination was 44 8 years i e almost 3 years higher than that found in the total series of isolated mitral stenosis

Rheumatic infection had been present in 17 patients 16 who had had rheumatic fever and 1 who had had chorea minor 10 out of the 17 patients had had rheumatic recurrences (59 per cent) including 5 with more than 1 recurrence The average age at the first infection was 15 4 years

The *heart symptoms* had set on at ages between 5 and 55 years The average age at the time of onset was 28 2 years

Two patients had had acute pulmonary oedema 5 had had pneumonia 2 had had pulmonary infarction and 5 had had arterial emboli (all cerebral in the systemic circulation prior to the first observation

Auricular fibrillation was ascertained in 18 patients and *right heart failure* in 10 at the first examination

Twelve patients belonged to *Class III* 9 to *Class IV* at the first observation

Roentgenologic examination was made in 18 patients The cardio thoracic index was over 50 in all cases in 1 from 51 to 54 in 9 between 55 and 64 and in 8 over 64 The left atrium was visibly enlarged in 16 patients the last two patients had not been examined in the right anterior oblique position or in lateral positions The possibility of enlargement of the atrium cannot therefore be excluded in these cases

In all cases but one the roentgenogram showed a straight left border of the heart or bulging of the second left arch

Clinical examination revealed a systolic apical murmur in 19 patients In 4 patients of this group a doubtful diastolic murmur had been heard at the apex but a definite diastolic or presystolic murmur had been found in no

case A mitral snap had been heard in 6 patients and accentuation of the first sound at the apex was mentioned in one

The *electrocardiograms* in 11 patients showed a QRS axis to the right of +90 degrees 3 with a QRS axis between +120 and +150 degrees and 8 with a QRS axis between +90 and +120 degrees

In 4 patients the QRS axis was between +90 and +60 degrees in 5 between +60 and +30 degrees and in 1 between 0 and +30 degrees The cases with right axis deviation include 2 cases with right bundle branch block

As already mentioned 18 patients had auricular fibrillation and 3 had sinus rhythm The P waves were normal in these cases

The *arterial blood pressure* was higher than 150/90 mm Hg in 4 cases the highest being 150/110 mm Hg Thus the arterial tension was scarcely higher in any case than permissible according to age

The late course

All patients of this group had died either at home or in hospital at the time of the follow up As already mentioned no case had been autopsied

Age at death – 1 patient died between the 20th and 29th years 2 between the 30th and 39th years 8 between the 40th and 49th 8 between the 50th and 59th and 2 between the 60th and 69th years The average age at death was 47 9 years i e the same as in isolated mitral stenosis in the present series

Causes of death – 16 patients died of heart failure 1 of acute pulmonary edema 2 of cerebral embolism and 2 of pneumonia

The *survival time* after the first rheumatic infection averaged 32 5 years and the survival after the onset of the first heart symptom averaged 19 7 years

Course of the disease – *Auricular fibrillation was ascertained in all patients* of this group before death The survival time after this finding averaged 4 3 years it may be mentioned that 3 patients survived more than 10 years with auricular fibrillation the longest survival being 15 years

Right heart failure was ascertained before death in 17 patients The average survival time after this symptom was 2 5 years 1 patient survived 14 years with right heart failure

Acute pulmonary oedema was the cause of death in a woman aged 60 3 patients in all of this group had acute pulmonary oedema

Pulmonary infarction occurred during the late course in 1 patient so that this complication was present in 3 cases in all

Of the five patients with cerebral emboli before the first observation 2 had recurrences during the late course Four other patients developed arterial emboli in 3 cases cerebral and in 1 case renal *emboli 2 patients died of cerebral emboli* and a third patient died of heart failure in conjunction with cerebral emboli For patients with past first embolism the survival time averaged 5 years and only 1 of these patients survived more than 10 years

Patients classified in Class III had an average survival time of 5 2 years for patients with sinus rhythm 6 years and for those with auricular fibrillation 5 years The survival time for patients in Class IV averaged 0 7 years

It appears from the preceding section that this group of 21 patients with clinically supposed but not verified mitral stenosis bears a very close re semblance to the series of isolated mitral stenosis This applies to all essential points in the course of the disease such as the nature and the frequency of complications survival times after important events and duration of life prognostically this group cannot be distinguished from the series of diagnosed cases

Chapter VI

Mitral Stenosis Combined with Aortic Valvular Disease

As a supplement to the main subject of the present study an investigation of the course of isolated mitral stenosis mention is made in this chapter of mitral stenosis combined with aortic valvular disease (aortic disease) The survey of this group is given on the same lines as were used in describing isolated mitral stenosis the greatest importance being attached to a comparison between the course of the disease in the two groups

Definition of the series

This series comprises 59 patients 49 were included on the basis of the clinical diagnosis of mitral stenosis combined with aortic disease established at the first observation 10 patients were included on the basis of the autopsy diagnosis

The criteria for the clinical diagnosis of mitral stenosis combined with aortic disease were described in detail on pages 31 to 32 The safety of this diagnosis was mentioned on pages 34 to 36 and it was pointed out that the clinical diagnosis of mitral stenosis combined with aortic disease in the present series as well as in the literature is somewhat more doubtful than the diagnosis of isolated mitral stenosis Owing to the difficulties in establishing the clinical diagnosis the distinction between the two forms will not be quite certain

With regard to the clinical diagnosis the group mitral stenosis combined with aortic disease only includes cases in which this diagnosis was clinically established at the first examination The few cases in which complicating aortic disease was not clinically ascertained until at the follow up have been included in the group isolated mitral stenosis as these had been considered cases of isolated mitral stenosis in the course of time had only had the characteristics of mitral stenosis and possibly had not developed the aortic disease until at a late stage

PRESENT SERIES AT THE FIRST EXAMINATION

Sex and age

The series of 59 patients was composed of 28 males and 31 females i e an almost equal sex incidence in contrast with the great preponderance of females in the cases of isolated mitral stenosis

The age incidence is shown in Table 63 The youngest patient was 14 years

the oldest 73 The great majority were between 30 and 60 years and 16 pa tients in all were over 50 (27 per cent) The average age was 42 5 years in either sex at the first observation

TABLE 63

Age and Sex at First Observation in Mitral Stenosis with Aortic Valvular Disease

Age	Female	Male	Total
14–19 years	1	1	2
20–29	4	2	6
30–39	6	10	16
40–49	12	7	19
50–59	6	6	12
60–69	1	1	2
70–79	1	1	2
Total	31	28	59

Past rheumatic infection

A past history of rheumatic infection was known in 42 patients (71 6 per cent) *38 had had rheumatic fever 4 chorea minor 24 patients (57 per cent)* had had rheumatic recurrences Further details are mentioned in the section *on rheumatic infection in the course of mitral stenosis with aortic disease*

The onset of the heart symptoms varied between the extremes 7 and [illegible]1 years The average age at the onset of the first symptom was 31 2 years and the average duration of the symptoms at the first observation was thus 11 3 years

In 54 patients the heart symptom set on in the form of dyspnoea on exertion or by night Palpitation was the first symptom in 3 angina pectoris in 1 and haemoptysis in 1 patient

Acute pulmonary oedema or cardiac asthma had occurred before the first observation in 10 patients 5 had had haemoptysis and 2 had had definite pulmonary infarctions Arterial emboli in the systemic circulation had been present in 5 patients cerebral emboli in 4 cases and emboli in the extremities in 1

Precordial pain of the same nature as in angina pectoris had occurred in [illegible] patients (12 per cent) and syncopes in 5 (9 per cent)

Cardiac State at the First Observation

As in the case of isolated mitral stenosis the description of the cardiac state will comprise the heart rhythm right heart failure heart size and degree of physical activity

Heart rhythm – 31 patients had sinus rhythm whereas 28 had auricular fibrillation (47 per cent) paroxysmal in 1 case and chronic in 27 cases

TABLE 64

Heart Rhythm in the Various Age groups at the First Examination

Age	Number of patients total	Number of patients with auricular fibrillation	
14 19 years	2	–	–
20–29	6	–	–
30–39	16	7	44
40–49	19	11	8
50–59	12	8	67
60–69	2	–	–
70–79	2	2	100
Total	59	28	47

It appears from Table 64 that mitral stenosis with aortic disease shows the same tendency to increasing frequency of auricular fibrillation with advancing age as isolated mitral stenosis

Right heart failure – This was ascertained in 15 patients (25 per cent) 7 were over 50 years of age and 12 had auricular fibrillation

Heart size – 7 out of 53 patients examined roentgenologically had cardiothoracic indices under 51 one had an index between 51 and 54 34 had indices between 55 and 64 and 11 were over 64

TABLE 65

Heart Size in Relation to Heart Rhythm

Cardiothoracic index	Sinus rhythm	Auricular fibrillation	Total
under 51	7	–	7
51–54	–	1	1
55–64	16	18	34
65 or more	5	6	11
Total	28	25	53

Table 65 shows that all cases with a cardio thoracic index under 51 had sinus rhythm and that only one patient with auricular fibrillation had an index under 55 In both forms of heart rhythm there was a considerable number of patients with cardio thoracic indices over 55 and no small number with indices over 65 12 patients with right heart failure all had cardio thoracic indices over 55

In the group of mitral stenosis with aortic disease auricular fibrillation was almost always associated with a cardio thoracic index over 54 and cases with right heart failure very often presented auricular fibrillation and always had cardio thoracic indices over 54 These tendencies in the development of the heart disease are in complete accord with the findings in cases of isolated mitral stenosis

When compared to the latter cases the group of mitral stenosis with aortic disease showed a tendency to a higher cardio thoracic index in most cases This was also to be expected as a number of the patients with complicating aortic disease showed signs of enlargement of the left ventricle

Degree of physical activity

Sixteen patients of this group belonged in Class II (27 per cent) 29 in Class III (49 per cent) and 14 in Class IV (24 per cent) This does not differ much from the distribution of the cases of isolated mitral stenosis

With regard to the four main points in the cardiac state the distribution of cases of mitral stenosis with aortic disease is thus in all essentials in accord with the findings in cases of isolated mitral stenois

Electrocardiographic Findings

The most important of these auricular fibrillation was mentioned above

P waves

Three out of 31 patients with sinus rhythm had P waves of a duration longer than 0 13 second There were no cases with abnormally tall P waves or with abnormal splitting of these The incidence of abnormal P waves among patients with sinus rhythm was thus 9 per cent this is lower than in cases of isolated mitral stenosis where abnormal P waves occurred in 30 per cent

The P R interval – This was longer than 0 22 second in 2 out of 31 patients One had a rheumatic recurrence In the other case no cause of the prolongation of the P R interval could be demonstrated

The QRS axis – The distribution of the QRS axis is given in Table 66 It shows that 5 patients had right axis deviation 11 had a QRS axis between

0 and +90 20 between +30 and +60 12 between 0 and 30 whereas 1 patients had a QRS axis between −30 and 0 and 2 were between −60 and 30 degrees

TABLE 66
QRS Axis in 59 Cases of Combined Mitral and Aortic Valvular D

QRS axis	Number of pat	
+90 − +1 0	5	8
+60 − +90	11	19
+30 − +60	20	34
0 − +30	17	0
− 0 − 0	9	15
−60 − −30	2	3
Total	59	100

In most cases of combined mitral and aortic disease the QRS axis was thus between 0 and +90 degrees To elucidate the diagnostic value of the QRS axis in assessment of the degree of mitral stenosis and aortic valvular disease respectively when these occur simultaneously the following observations may be mentioned Autopsy was performed in all 5 cases with right axis deviation All showed pronounced mitral stenosis 2 had a pronounced aortic stenosis 2 a slight aortic stenosis and 1 showed pronounced *aortic incompetence* There was however an additional complication in 4 cases as 3 had tricuspid stenosis and the fourth had an adherent pericardium In this group of combined mitral and aortic disease *right* axis deviation in the limb leads thus did not exclude the presence of a severe aortic disease but they all had a severe mitral stenosis simultaneously and 4 out of 5 cases had yet another complication either tricuspid disease or adherent pericardium

Six of the patients with left axis deviation in the limb leads were autopsied They all had a severe *aortic valvular disease* in 5 there was a severe stenosis and the sixth had stenosis combined with incompetence 3 out of these 6 patients had a severe mitral stenosis as well 3 had a slight mitral stenosis In this group left axis deviation thus did *not* exclude the presence of a severe mitral stenosis though pronounced aortic valvular disease was always present simultaneously

T waves

From the previously mentioned criteria according to which the T waves are estimated 26 patients had normal T waves 5 had a negative T_1 1 had negative T_1 and T_2 17 had an iso electric T_1 and 10 had a negative T_1

TABLE 67

T Wave Changes in Relation to QRS Axis and Heart Rhythm

	QRS +90 – +120		QRS 0 – +90		QRS -60 – 0		Total	
	SR	AF	SR	AF	SR	AF	SR	AF
Normal T waves	2	–	13	10	–	1	15	11
T_3 negative	–	–	2	2	1	–	3	2
T_2 and T_3 negative	–	1	–	–	–	–	–	1
T_1 iso electric	2	–	5	7	1	2	8	9
T_1 negative	–	–	3	1	2	4	5	5
Total	4	1	23	20	4	7	31	28

SR = sinus rhythm
AF = auricular fibrillation

It appears from Table 67 that changes in the T waves were of almost the same frequency in sinus rhythm and in auricular fibrillation 15 out of 31 patients with sinus rhythm had normal T waves 3 had a negative T_3 8 an iso electric T_1 and 5 a negative T_1 11 out of 28 patients with auricular fibrillation had normal T waves 2 had a negative T_3 1 had negative T and T_3 9 had a iso electric T_1 and 5 had a negative T_1

A negative T_1 was seen only with QRS axes of 0 – +90 and -60 – 0

Except for the more frequent occurrence of a negative T_1 the T wave changes in this group do not differ from the changes in the group of isolated mitral stenosis

Bundle branch block – This occurred in 2 cases A man aged 52 had left bundle branch block 1 year later autopsy revealed a very pronounced aortic stenosis and a slight mitral stenosis A woman aged 42 had right bundle branch block in this case autopsy showed a very pronounced mitral stenosis combined aortic stenosis and incompetence and adherent pericardium

Roentgenologic Findings

Roentgenologic examination was performed in 53 out of 59 patients in 8 in the form of orthodiagraphy in 45 as roentgenography

The cardio thoracic index has already been mentioned In the following it may be mentioned to what extent the roentgenologic examination contributed to the clinical diagnosis of mitral stenosis with aortic disease

Enlargement of the left atrium

At the first examination exposures were made in 8 cases in the right anterior oblique position enlargement of the left atrium was demonstrated in all these cases In 4 the atrium was distinctly visible in the exposure in the postero anterior position

In 21 out of 45 patients examined solely in the postero anterior position the left atrium was enlarged whereas this could not be demonstrated in 24 patients 8 patients of the group in which enlargement of the left atrium was not demonstrated at the first examination were examined at the follow up in the right anterior oblique position the left atrium was enlarged in 5

Enlargement of the left atrium was thus demonstrated in 13 in all out of 16 patients (81 per cent) examined in the right anterior oblique position

Straight left contour of the heart or bulging of the second left arch

At the first observation the left contour of the heart was straight or the second left arch bulging in 35 out of 53 patients (66 per cent) whereas there was no effaced waist of the heart in 18 cases Enlargement of the left atrium was found in 8 of the latter patients including 6 in whom it was seen only in the right anterior oblique position

The roentgenograms taken at the first examination thus lent support to the diagnosis of mitral stenosis in a total of 43 out of 53 patients or in about four fifths of cases examined roentgenologically

At the first observation 10 out of the 53 patients showed neither enlargement of the left atrium nor a straight left border of the heart with or without bulging of the second left arch in about one fifth of the cases the roentgenologic examination was thus non contributory It may however be mentioned that these patients had not been examined in the right anterior oblique position

It may be added that 12 patients of this group were examined at the follow up in the postero anterior position and in the right anterior oblique position in 9 out of 12 enlargement of the left atrium could be demonstrated and in 8 out of 12 the left border of the heart was straight or the second left arch bulged A total of 10 out of 12 patients presented at least one of these signs so that examinations in the right anterior oblique position at the follow up also supported the clinical diagnosis of mitral stenosis in four fifths of the cases

Enlargement of the left ventricle

Enlargement of the left ventricle i e enlarged or lengthened inferior left arch in the postero anterior position was found in 35 out of 53 patients examined (two thirds of the cases)

The diagnosis of the complicating aortic disease was thus supported roentgenologically in two thirds of the cases

Arterial blood pressure

It may be mentioned that the arterial blood pressure in 11 out of 59 patien was 150/90 mm Hg or more (19 per cent) Only one patient presented a pro nounced rise in the blood pressure (B P = 240/140 mm Hg)

RESULTS OF THE FOLLOW UP

This section gives a survey of the series of mitral stenosis combined with aortic disease as it appeared at the follow up after a period of observation varying from 3 to 20 years

At the time of the follow up 47 patients had died (80 per cent) and 1[illegible] survived (20 per cent)

Survey of patients who died during the period of observation

Age at death

The youngest patient died at the age of 14 years the oldest at the age of 7[illegible] The distribution of the series according to age at death is shown in Table 68 The average age at death was 48 4 years for both sexes in males 46 8 years and in females 51 0 years

TABLE 68

Distribution of Mitral Stenoses with Aortic Valvular Disease according to Age at Death

Age	14 19	20–29	30–39	40–49	50–59	60–69	70–79 years	Total
Males	1	1	5	8	7	3	1	26
Females	–	–	2	7	9	2	1	21
Total	1	1	7	15	16	5	2	47
Cumulative %	2	4	19	51	85	96	100	–

The greatest number of deaths occurred in the age groups 40–49 and 50–59 and a total of 49 per cent of the patients died after the age of 50

Causes of death

The classification according to causes of death was undertaken on the lines mentioned in cases of isolated mitral stenosis Table 69 gives a survey of the frequency of the various causes of death

A total of 98 per cent. of this group died of heart failure thrombo embolic complications or intercurrent infections whereas only 1 patient (2 per cent) died of a different cause. This was a woman aged 65 who died of metastases from carcinoma of the breast. 66 per cent died of heart failure and 19 per cent. of thrombo embolic complications. Death of infections occurred in 13 per cent: 7 per cent of pneumonia, 4 per cent of subacute bacterial endocarditis and 2 per cent of rheumatic fever. The last case was that of a boy aged 14 who died in the third rheumatic recurrence.

TABLE 69

Causes of Death in Mitral Stenosis Combined with Aortic Valvular Disease

	Number of patients	
Heart failure		31 = 66 %
Congestive failure	21	
Acute pulmonary oedema	3	
Sudden death	2	
Heart death	5	
Thrombo embolic complications		9 = 19 %
Cerebral emboli	4	
Other arterial emboli	1	
Pulmonary embolism	4	
Infections		6 = 13 %
Active rheumatic fever	1	
Subacute bacterial endocarditis	2	
Sepsis	–	
Pneumonia	3	
Other causes of death		1 = 2 %
		47 = 100 %

With regard to age at death and causes of death this group is in accord with the series of isolated mitral stenoses.

Autopsy findings

Table 70 gives a survey of the autopsy findings in [illegible] cases of mitral stenosis combined with aortic disease. From the available descriptions of the autopsy findings it was found, as shown in the table, that 11 cases had a pronounced mitral stenosis and a pronounced aortic valvular disease, 4 cases had a pronounced mitral stenosis with slight aortic valvular affection and 4 cases had

a pronounced aortic valvular disease with slight mitral stenosis Both valvular diseases were slight in 2 cases

Tricuspid stenosis was found in 4 out of 21 cases (about 20 per cent) In cases of isolated mitral stenosis only 5 with tricuspid stenosis were found among 85 autopsied cases (6 per cent) Even though the figures are small it is worth mentioning that this finding is in conformity with the general experience that tricuspid stenosis is relatively more frequent in cases of combined mitral and aortic valvular disease than in isolated mitral stenosis (*Stone and Feil Graham et al*) Further in 1 patient distinct traces of past endocarditis of the tricuspid valves were found though no valvular disease could be demonstrated

TABLE 70

Autopsy Findings in 21 Cases of Mitral Stenosis combined with Aortic Valvular Disease

Title	14–19 1	20–29 –	30–39 2	40–49 7	50–59 9	60–69 1	70–79 years 1	Total 1
Pronounced mitral stenosis and pronounced aortic disease	1	–	–	5	5	–	–	11
Pronounced mitral stenosis and slight aortic disease	–	–	1	–	1	1	1	4
Slight mitral stenosis and pronounced aortic disease	–	–	1	1	2	–	–	4
Both forms of valvular disease slight	–	–	–	1	1	–	–	2
Calcification in mitral valves	–	–	2	3	2	–	–	7
Calcification in aortic valves	–	–	1	3	2	–	–	6
Tricuspid stenosis	1	–	1	1	1	–	–	4
Sequelae of tricuspid endocarditis	–	–	–	–	1	–	–	1
Adherent pericardium	–	–	–	1	–	1	–	2
Coronary sclerosis	–	–	–	1	3	1	1	6

The ages at death of patients with tricuspid stenosis were 14 37 49 and 50 years averaging 37 5 years thus somewhat lower than the average for the whole group

Adherent pericardium was seen in 2 patients

Coronary sclerosis was described in 6 patients chiefly in the older age groups A healed myocardiac infarction was found in a man aged 67

Kidney diseases were described in 11 cases In 9 there were signs of recent or healed kidney infarctions and 2 had other kidney affections nephrosclerosis in 1 case and chronic pyelonephritis in 1 case

Summarizing it can be ascertained that the series of mitral stenoses combined with aortic valvular disease was in accord at autopsy with the experiences previously mentioned in the sections on autopsied cases of isolated mitral stenosis

Survey of survivors

The twelve surviving patients were all followed up by the writer The period of observation varied from 3 to 20 years averaging 8 7 years

The most important data concerning the follow up of these patients are given in Table 71

TABLE 71

Survey of Follow up of 12 Patients with Mitral Stenosis and Aortic Valvular Disease

	20–29	30–39	40–49	50–59	60–69	70–79 y	Total
Males	–	1	1	–	–	–	2
Females	1	3	3	1	1	1	10
Total	1	4	4	1	1	1	12
Class II	–	2	2	–	1	1	6
Class III	1	1	1	1	–	–	4
Class IV	–	1	1	–	–	–	2
Sinus rhythm	1	3	2	1	1	1	9
Auricular fibrillation	–	1	2	–	–	–	3
Right heart failure	–	–	1	–	–	–	1
Cardio thoracic index –	1	1	–	–	1	1	4
51 54	–	2	4	1	–	–	7
55–64	–	1	–	–	–	–	1
65 or more							

The table shows that a comparatively great number of patients were under 40 years of age correspondingly the average age of the patients with mitral and aortic disease followed up (43 6 years) was somewhat lower than that of patients with isolated mitral stenosis followed up (49 years)

A higher percentage of the patients followed up were in a less advanced phase of the heart disease a fact which is also in accord with the lower average age

Half the patients belonged to Class II and were thus fit for work *Only* one fourth had auricular fibrillation and only 1 patient had right heart failure

The cardio thoracic index was over 50 in all cases in 8 over 55 and in 1 over 65

Signs of progression of the heart disease were seen in few cases only In 6 the condition had remained subjectively and objectively unchanged 1 patient had developed auricular fibrillation 1 presented right heart failure and in 4 other patients the capacity for work was reduced although corresponding objective signs of aggravation could not be ascertained

Progression of the heart disease was thus not so pronounced nor so frequent as among cases of isolated mitral stenosis it should however be considered that the period of observation in cases of mitral stenosis with aortic disease was shorter and that this group had a lower average age than patients with isolated mitral stenosis followed up

RHEUMATIC INFECTION AND THE COURSE OF MITRAL STENOSIS COMBINED WITH AORTIC VALVULAR DISEASE

As previously mentioned 42 out of 59 patients of this group had a past history of rheumatic infection (71 6 per cent) 38 patients had had rheumatic fever and 4 had had chorea minor The rheumatic infection had been present in 20 males and 22 females i e with the same frequency in either sex

Twenty four patients (57 per cent) had had rheumatic recurrences and 12 in all had had 3 or more recurrences (29 per cent)

The average age at the first rheumatic infection was 12 5 years

Rheumatic infection had been diagnosed in about 72 per cent of cases of mitral stenosis with aortic valvular disease and in 58 per cent of cases of isolated mitral stenosis in the present series The average age at the first infection was 12 5 years in the former cases as compared to 15 4 years in the latter This tendency to an earlier and more frequent rheumatic infection among cases of combined mitral and aortic disease than in those of isolated mitral stenosis is in accord with the findings in *Wilson*s and *DeGraff and*

Lingg's series of rheumatic heart disease from North America and in Coombs's series of rheumatic heart disease from England (*Wilson* 1940 *DeGraff and Lingg* 1934 *Coombs* 1924)

The *survival time* after the initial rheumatic infection varied between such wide limits as 5 and 49 years The average survival time of those who died during the period of observation was 33 6 years and that of the survivors was 31 0 years The duration of life among patients with rheumatic infection averaged 48 1 years in the case of those who died and 40 7 years in the case of survivors

These figures do not differ much from the findings in the group of cases of isolated mitral stenosis

AGE AT ONSET OF THE HEART SYMPTOMS

The average age when the first heart symptom appeared in the present series was 31 2 years It was somewhat higher in males 33 7 than in females 28 / years

The *survival time* after the first heart symptom averaged 14 9 years in the group of patients who died 12 7 in the case of males and 17 7 years in the case of females in the group of survivors it averaged 18 5 years 18 0 in males and 18 6 in females These findings correspond to the experiences in the cases of isolated mitral stenosis

AURICULAR FIBRILLATION IN THE COURSE OF MITRAL STENOSIS WITH AORTIC VALVULAR DISEASE

Auricular fibrillation was definitely ascertained in the course of the disease in 36 out of 59 patients (61 per cent) When 4 cases with insufficient data are left out a total of 65 per cent have had auricular fibrillation

Of patients who died during the period of observation 33 out of 43 with sufficient data had had auricular fibrillation ascertained (77 per cent) this incidence is only slightly lower than that of auricular fibrillation in cases of isolated mitral stenosis (84 per cent)

The ages when *auricular fibrillation* was ascertained appear from Table 72 it shows that *33 per cent* had developed this complication before the 40th year *39 per cent* between the 40th and 49th years and 27 per cent after the 50th year

TABLE 72

Age at Onset of Auricular Fibrillation

Age	Number of patients	%
20–29 years	1	
30–39	11	33
40–49	14	
50–59	8	39
60–69	1	
70–79	1	27
Total	36	100

The average age when auricular fibrillation was ascertained was 48 8 years this corresponds to the finding in cases of isolated mitral stenosis

TABLE 73

Survival of 36 Patients Calculated from the Time when Auricular Fibrillation was ascertained

Year of observation	0 1	1 2	2 3	3 4	4 5	5 6	6 7	7 8	9 10	10 11	11–12	12 13
Survival percentage	100	69	64	52	41	38	30	22	15	8	8	8

The survival after auricular fibrillation was ascertained is shown in Table 73 it appears that 69 per cent survived after the 1st year 38 per cent after the 5th year and 8 per cent after the 10th year The median survival time is between 3 and 4 years this is somewhat lower than that found in cases of isolated mitral stenosis with auricular fibrillation

RIGHT HEART FAILURE DURING THE COURSE OF THE DISEASE

Right heart failure was present in 15 patients at the first observation and developed in 21 during the period of observation so that a total of 36 out of 59 patients presented this sign (61 per cent) When 6 cases with insufficient data are left out 68 per cent in all had had right heart failure

In the group of patients who died during the period of observation 35 out of 41 with sufficient data (85 per cent) had had right heart failure

Right heart failure was thus as frequent in this group as in cases of isolated mitral stenosis

The ages when right heart failure was ascertained appear from Table 74 It shows that this syndrome was ascertained before the 40th year in 20 per cent between the 40th and 49th years in 42 per cent and not until after the 50th year in the rest of the cases

TABLE 74

Age when Right Heart Failure was ascertained

Ag	N mb of p t t	
14–29 years	2	6
30–39	5	14
40–49	15	42
50–59	12	32
60–79	1	3
70–79	1	3
Total	36	100

The average age when right heart failure was ascertained was 45 6 years the same as in cases of isolated mitral stenosis

The *survival times* after development of right heart failure are shown in Table 75 Half the patients died within the first year 19 per cent were alive after 5 years and all were dead after 10 years

The survival times after development of right heart failure in mitral stenosis with aortic disease were thus somewhat shorter than those found in cases of isolated mitral stenosis as about 10 per cent of the latter survived more than 10 years

TABLE 75

Survival of 36 Patients after Right Heart Failure had been ascertained

Year of observation	0 1	1	2–3	3–4	4–5	5–6	6 7	7 8	8–9	9 10	10–11
Survival percentage	100	50	50	35	26	19	14	14	14	7	0

CARDIAC ASTHMA AND ACUTE PULMONARY OEDEMA

This syndrome was present in 18 out of 59 patients (30 per cent) and was thus more frequent than in cases of isolated mitral stenosis

Acute pulmonary oedema was the cause of death in 3 cases

Cardiac asthma and acute pulmonary oedema were present at all ages between 26 and 71 years The average age at the first attack was 40 1 years 7 patients had had repeated attacks

The survival after the first attack appears from Table 76

TABLE 76

Survival of 18 Patients with Cardiac Asthma and Acute Pulmonary Oedema

Year of observation	0–1	1–2	2–3	3–4	4–5	5–6	6–7	7–8	8–9	9–10	10–11	11–12
Survival percentage	100	72	66	60	60	53	40	32	24	24	16	16

It appears that about one fourth died within the first year after the beginning of the attacks 53 per cent survived after 5 years and 16 per cent after 10 years

Cardiac asthma and acute pulmonary oedema were thus more frequent in this group than in cases of isolated mitral stenosis and the prognosis in cases with these attacks was more serious in mitral stenosis combined with aortic valvular disease than in isolated mitral stenosis

ISOLATED HAEMOPTYSIS

This occurred in 5 patients The average age was 21 years All patients died in from 4 to 15 years averaging 8 years after the first haemoptysis

PULMONARY INFARCTION

This complication had been present in 14 patients (24 per cent) All patients died 12 within 1 year and 2 in the course of 2 and 7 years after the pulmonary infarction In most cases it was thus a complication setting on during the terminal stage as in cases of isolated mitral stenosis

ARTERIAL EMBOLISM IN THE SYSTEMIC CIRCULATION

Arterial embolism in the systemic circulation developed in a total of 10 patients of this group (17 per cent) and had been present in 9 out of 47 who died (19 per cent)

The complication developed in 6 males and 4 females The age at the onset of the first attack was from 40 to 49 years in 6 patients and from 50 to 59 years in 4

Localization of emboli

Cerebral emboli occurred 10 times in all in 8 patients emboli in abdominal vessels were present 7 times in all in 4 patients (splenic emboli in 4 renal emboli in 1 liver emboli in 1 and emboli of the superior mesenteric artery in 1) emboli of the iliac artery were seen in 1 patient and in vessels of the limbs in 2 (the popliteal artery in 1 the brachial artery in 1)

Five patients had *embolic recurrences* 2 had 2 attacks in all and 3 patients had 3 attacks The intervals between the first attack and the recurrences were 7 years at most and often shorter than 1 year

Factors predisposing to emboli

All the ten patients had auricular fibrillation when they first developed arterial embolism 7 patients had right heart failure and 7 were under continuous treatment with digitalis The size of the heart when embolism first set on was known in 8 cases the cardio thoracic index was over 55 in all

Lethality in cases with arterial embolism

Three out of the ten patients with embolism died in the first attack 2 of cerebral emboli and 1 of emboli in abdominal vessels 5 out of the 7 survivors died later 1 of recurring cerebral embolism after 1 year 4 of congestive failure after 1 2 3 and 7 years 2 patients survived 2 years after the first attack

Arterial embolism was of somewhat rarer occurrence in the series of combined mitral and aortic valvular disease than in the cases of isolated mitral stenosis However when arterial embolism developed in the systemic circulation in the former cases the prognosis was just as grave as in the latter

PREGNANCY IN THE COURSE OF MITRAL AND AORTIC VALVULAR DISEASE

Of 31 women in the series 17 in all (55 per cent) have been pregnant and 15 (48 per cent) gave birth to one or more liveborn children 4 women delivered one liveborn child 2 had 2 liveborn children 5 had 3 liveborn children

3 had 5 and one had 7 liveborn children Abortion was induced in 2 case spontaneous abortion occurred in 2 cases and one child was stillborn

Death in conjunction with pregnancy or parturition did not occur in th series Permanent aggravation of the heart disease was seen in 2 cases (or I per cent of all pregnant women)

COMPLICATING DISEASES IN THE COURSE OF MITRAL AND AORTIC VALVULAR DISEASE

Carcinoma of the breast was the cause of death in 1 case

Pulmonary tuberculosis was ascertained in 1 patient

Exophthalmic goitre was present in 1 patient

Duodenal ulcer occurred in 1 case

"Shaking palsy was seen in 1 case

Subacute bacterial endocarditis cured with penicillin treatment had com plicated the course in 1 case

Syphilis in the past history occurred in 1 case At autopsy no signs of syphilitic heart disease were found Wassermann s test was negative in 47 examined cases

SURVIVAL AFTER THE FIRST OBSERVATION

The survival after the first observation in mitral stenosis with aortic valvular disease is shown in Table 77

TABLE 77

Survival after First Observation of all Cases of Mitral Stenosis with Aortic Valvular Disease

Year of observation	0–1	1–2	2–3	3–4	4–5	5–6	6–7	7–8	8–9	9–10	10–11	11–12
Survival percentage	100	73	61	53	49	4	35	35	31	29	6	6

Year of observation	12–13	13–14	14–15	15–16	16–17	17–18	18–19	19–20	0–1
Survival percentage	26	24	24	18	18	14	11	7	7

Seventy three per cent survived after 1 year 45 per cent after 5 years 26 per cent after 10 years 18 per cent after 15 years and 7 per cent after 20 years The median survival time for the whole group is between 3 and 4 years

The group of combined mitral stenosis and aortic valvular disease shows a greater earlier fall in the survival than that of cases of isolated mitral stenosis but with regard to the long term survival it is in fairly good accord with the latter group this also appears from Fig 18 page 160

When considered according to the prognostic classification used for cases of isolated mitral stenosis the group of mitral stenosis with aortic valvular disease shows exactly the same tendencies as were found in cases of isolated mitral stenosis

Of 14 patients in main group A i e patients with sinus rhythm in Class II 46 per cent survived after 10 years

Of 14 patients in main group B i e patients with sinus rhythm in Class III 17 per cent survived after 10 years

Of 18 patients in main group C i e patients with auricular fibrillation in Classes II and III 14 per cent survived after 10 years

Of 13 patients in main group D i e patients in Class IV all were dead after 4 years

In main groups A and D the findings corresponded exactly to those in the group of isolated mitral stenosis Main groups B and C showed exactly the same tendency as the group of isolated mitral stenosis though the survival found was somewhat lower than that of the latter group

Summing up it can be ascertained that it has been found in the present series of cases that with regard to the course of the disease mitral stenosis with *aortic* valvular disease in all essentials differs but slightly from cases of isolated mitral stenosis It was found however that the survival time after auricular fibrillation *and right* heart failure had been ascertained tended to be shorter than that of cases of isolated mitral stenosis this tendency was also found to apply to cases in more advanced stages of the disease when a prognostic classification was attempted on the basis of the condition of the patients at the first observation

Notes in Conclusion

In a total assessment of the results of the follow up compared with the condition of the patients at the first observation it is conspicuous that the great majority of cases showed signs of progression of the heart disease during the period of observation This applies to cases of isolated mitral stenosis of clinically probable mitral stenosis as well as to those of mitral stenosis with aortic valvular disease

The lethality during the period of observation was exceedingly high as 70 per cent of cases of isolated mitral stenosis and 80 per cent of those of combined mitral and aortic valvular disease had died at the time of the final assessment of results

The estimate based on the condition at the first observation comprised the establishment of four main groups showing distinct differences with regard to the late prognosis This classification may be briefly described as far as cases of isolated mitral stenosis are concerned

Group A i e patients with sinus rhythm belonging in Class II comprises about one sixth of the series and showed a very high survival rate during the period of observation The median survival time in this group was many years (> 20 years) Among the survivors 60 per cent showed symptoms or signs of progression of the heart disease at the follow up whereas the condition had remained unchanged in 40 per cent

Group B i e patients with sinus rhythm belonging in Class III comprise about one fourth of the series and showed an evenly and rapidly falling survival The median survival time in this group was from 5 to 6 years in males and from 7 to 8 years in females Among the survivors 60 per cent showed evidence of progression of the heart disease at the follow up whereas the condition had remained unchanged in 40 per cent

Group C i e patients with auricular fibrillation belonging in Classes II and III comprises over one third of the series and showed an evenly and rapidly falling survival during the period of observation The median survival time in this group was the same as in main group B from 5 to 6 years in males and from 7 to 8 years in females Among the survivors 60 per cent showed evidence of progression of the heart disease at the follow up whereas the condition had remained unchanged in 40 per cent

Group D i e patients in Class IV comprises about one fifth of the series and showed a very low survival rate during the period of observation The median survival time in this group was under 1 year

Reverting now to the present day problem which inspired the writer to the present study namely the modern surgical treatment of mitral stenosis it would be natural on the basis of the results of these investigations to decide on the timeliness of this operation

It is obvious that we cannot at present draw far reaching conclusions as to the indications for mitral valvulotomy as the periods of observation in cases already operated on are so short that it cannot yet be said whether the operation actually affords long term relief Assuming however that mitral valvulotomy has a lasting effect and that the lethality from the operation can be kept within reasonable limits it seems justifiable to conclude from the results of the present investigations that it must be considered as part of the treatment of isolated mitral stenosis as the prognosis in the case of medical treatment has been found to be so grave in most cases

It is especially the cases belonging in main groups B and C that will be considered suitable for mitral valvulotomy Main group B is the more important in this connection as the age of the patients in this group averaged 35 years at the first observation and half the patients died before the 43rd year of life

In main group C too mitral valvulotomy must be considered The average age at the first observation in this group was about 45 years and half the patients died before the 53rd year of life

In main group D surgical operation would actually be indicated but the risk would presumably be so great in this group that this form of treatment cannot be used

With regard to the timeliness of mitral valvulotomy in patients of group A this represents a special problem In this group we find so high a survival rate that the operation cannot be considered indicated for the whole group in general 40 per cent of the survivors showed an unchanged good condition at the follow up and these patients probably represent the benign cases of mitral stenosis attaining a great age with little heart trouble and should not be operated on On the other hand 20 per cent of group A died during the period of observation and 60 per cent of the survivors showed evidence of progression of the heart disease at the follow up *Whether patients of group A with* signs of progression of the heart disease should be operated on or not is one of the questions that remain to be decided in future

Summary

Introduction

The purpose of the present work is to afford a new contribution to the description of the course and prognosis of mitral stenosis

Chapter I

This chapter gives a brief survey of the historical development of our knowledge of mitral stenosis with special reference to its diagnosis and pathology

Chapter II

The main features of previous investigations into the prognosis of mitral stenosis are reviewed The only extensive systematic investigation has been undertaken by *Grant* who observed his series of ex servicemen for 10 years His series naturally comprised males only chiefly in the age groups between 20 and 40 years At the follow up about one third had died one third showed aggravation and one third had remained unchanged It is pointed out in conclusion that the literature contains no systematic studies on the course of mitral stenosis in older decades

Chapter III

The writer s investigations comprise a clinical analysis of the course of the disease in 351 patients with mitral stenosis They were first examined in the course of the period 1933–49 and traced from 1951 to 1953 the period of observation after the first examination thus varying from 3 to 20 years According to criteria mentioned the series is divided into 3 main groups 271 patients with isolated mitral stenosis 21 with clinically probable mitral stenosis and 59 with mitral stenosis and aortic valvular disease The series was derived from two sources 285 patients from *Medical Department B the University Hospital Copenhagen* and 66 patients from the *private consultation of Professor Erik Warburg M D*

A total of 931 patients died during the period of observation and 94 were alive at the time of the follow up Except for one patient who had emigrated it was managed to trace all patients at the final estimate It was managed to collect full details on the course of the disease in most of the patients who died during the period of observation and 90 out of 94 surviving patients were followed up by the writer In the case of the four patients who were not followed up sufficient details about their condition at the time of the examination were also procured

This chapter further describes the criteria for the clinical diagnoses and the reliability of the latter judged by the findings at autopsy or at the follow up Mention is made of the roentgenologic electrocardiographic and clinical criteria used

Finally the principles used in estimating the prognosis are mentioned These are based upon a total assessment of the survival after certain definite periods with due regard to survivors as well as to patients who died during the period of observation

Chapter IV

This chapter gives a detailed description of the clinical picture and of the whole course of the disease in 271 patients with *isolated mitral stenosis*

This group comprises 194 females and 77 males at an average age of 41 5 years at the *first examination* The great majority of the patients were between 30 and 49 years 26 per cent were over 50 years 59 per cent had had a rheumatic infection the average age at the first rheumatic infection was 15 4 years and the interval between the first infection and the first observation averaged 2, 4 years The average age when the first heart symptom set on was 31 2 years and the duration of the symptoms averaged 10 3 years at the first *observation* 57 per cent of the patients had auricular fibrillation and 25 per cent had right heart failure The size of the heart indicated by the cardio thoracic index showed very considerable variations 158 out of 181 females and 54 out of 70 males thus had cardio thoracic indices over 50 and several were over 65 An analysis showed that auricular fibrillation was almost always associated with a cardio thoracic index over 50 most frequently over 55 in the case of right heart failure 80 per cent of the cases presented auricular fibrillation and almost always a cardio thoracic index over 55

At the first observation 21 per cent of the patients were grouped in Class II according to physical activity 59 per cent in Class III and 20 per cent in Class IV A comparison was made between a classification according to physical activity and one according to heart rhythm heart size and signs of right heart failure It appeared that most patients of Class II had sinus rhythm low de

grees of cardio thoracic indices and no signs of right heart failure whereas almost all patients of Class IV had auricular fibrillation higher cardio thoracic indices and signs of right heart failure Patients in Class III represented an intermediate stage

Enlargement of the left atrium or a straight left contour of the heart possibly with bulging of the second left arch was demonstrated at the roentgenologic examination and lent support to the clinical diagnosis in almost all thoroughly examined cases

Electrocardiograms with the three standard leads were available in 260 cases 34 out of 114 patients with sinus rhythm presented abnormal P waves 29 per cent had right axis deviation and 3 per cent left axis deviation Abnormal T waves were frequent and were seen especially in the case of auricular fibrillation Bundle branch block was observed in 5 patients and low voltage in 2 The T wave changes were present in the great majority of cases of Classes III and IV

At the *follow up* after a period varying from 3 to 20 years averaging 12 years 189 patients (70 per cent) had died The average age at death was 47 0 years and 42 per cent had died after the 50th year The causes of death were heart failure in 62 per cent thrombo embolic complications in 22 per cent infections in 9 per cent and 8 per cent died of other causes Only 3 patients died of unquestionable rheumatic recurrence and this was possibly the cause of death in 4 other cases 4 patients died of subacute bacterial endocarditis 9 died of acute pulmonary oedema 85 out of the 189 patients who died were autopsied Tricuspid stenosis was found in 5 cases (6 per cent) adherent pericardium in 6 calcification of the mitral valves in 27 and atheromatosis or arteriosclerosis of the coronary arteries was revealed in 33 cases

Seventy eight out of 82 survivors were followed up the period of observation averaged 9 7 years The average age at the time of the follow up was 49 1 years 69 per cent had auricular fibrillation and 42 per cent presented right heart failure In 40 out of 71 roentgenographed patients (56 per cent) the cardio thoracic index had increased by more than 10 per cent and in 34 out of 78 cases (44 per cent) the patient was transferred at the follow up from Class II to Class III or IV Judged by the criteria mentioned a total of two thirds of the patients followed up showed signs of progression of the heart disease during the period of observation

In 1 out of the four cases that were not followed up details of definite progression of the heart disease were available

Detailed mention is made of the first *rheumatic infection* and the number of rheumatic recurrences in relation to the subsequent course of the disease

It is concluded that the number of rheumatic recurrences in the present series did not decidedly influence the survival time after the first infection The average duration of life was lower after early initial infection than after late infection The survival times after the initial infection averaged 30 1 years in the case of patients who died and 33 3 in the case of survivors

The average survival time after the *onset of the heart symptoms* was 14 3 years in the case of 181 dead patients and 20 5 years in 86 survivors The survival time varied from 1 to 52 years after the first symptom It is stressed that 31 out of 189 dead patients died within 5 years after the onset of the symptoms As was to be expected the median survival time after development of the heart symptoms was decreasing with advancing age at the onset of the first symptom

The presence of *auricular fibrillation* was verified in 84 per cent of the patients who died during the period of observation and in whom the heart rhythm was known and in 70 per cent of the surviving patients The average age when auricular fibrillation was ascertained was 43 8 years and on the average it was not ascertained until 27 years after the first rheumatic infection and 10 6 years after the first heart symptom developed 43 per cent of the patients had right heart failure when auricular fibrillation was demonstrated 39 per cent of the females and 21 per cent of the males survived 10 years after auricular fibrillation had been ascertained The median survival time after this complication had been demonstrated was from 6 to 7 years in the case of females and from 4 to 5 years in the case of males A total of 18 out of 271 patients had had paroxysmal auricular fibrillation which became chronic in 16 Paroxysmal tachycardia was demonstrated in 5 patients (5 per cent of the group with sinus rhythm)

Right heart failure demonstrated at physical examination was found in 81 per cent of patients with mitral stenosis who died and in 68 per cent of the whole series The average age when right heart failure developed was 45 6 years The average interval from the first rheumatic infection was 29 years and that from the first heart symptom was 13 2 years Right heart failure was associated with auricular fibrillation in 75 per cent of the cases The median survival time after right failure had been ascertained was 2 3 years but it is stressed that a group of 11 per cent had survived this complication 10 years or more In patients with sinus rhythm the survival time after right heart failure had been demonstrated was distinctly shorter than that of the whole group

The presence of *cardiac asthma and acute pulmonary oedema* was described in 45 out of 2?1 patients (1? per cent) The average age was 37 4 years at the first attack 6 patients died in the first attack and 3 died later in a recurrent attack Of patients who survived the first attack 68 per cent survived 5 years and 37 per cent 10 years Of patients under 50 years of age 46 per cent survived 10 years The risk of death in acute pulmonary oedema was calculated to be 3 per cent for the whole series and 8 per cent for patients with a past first attack The patients of this group had had a lower average age at death or at the follow up than the total series Cardiac asthma and acute pulmonary oedema were thus accompanying symptoms in the early course of mitral stenosis with regard to the duration of life this group had a somewhat graver prognosis than the great majority of cases in the present series

Haemoptysis which was not associated with cardiac asthma acute pulmonary oedema or pulmonary infarction occurred in 31 cases at an average age of 29 2 years at the first attack The survival after the first haemoptysis was 46 per cent after 10 years and apparently lower in the case of repeated haemoptysis Like cardiac asthma and acute pulmonary oedema haemoptysis was a accompanying symptom in the early course of mitral stenosis and these patients had a lower average duration of life than the great majority of cases it may however be mentioned that no deaths of haemoptysis occurred in the present series

Pulmonary infarction occurred in 55 patients (20 per cent of the series) and in 50 out of 189 patients who died (2? per cent) This complication most frequently developed in patients with auricular fibrillation right heart failure and high cardio thoracic indices The average age when pulmonary infarction developed was 45 1 years 44 per cent of clinically diagnosed cases died immediately after the first pulmonary infarction One half of the survivors developed recurrences and only one fourth survived after 10 years

Pneumonia has been described in 97 patients (36 per cent)

Haemosiderosis in the lungs was definitely demonstrated in only 1 out of 19? roentgenographed patients

Arterial emboli in the systemic circulation were observed in 75 patients (?8 per cent) and in 61 out of 189 patients who died (32 per cent) The average age when emboli first developed was 45 2 years 85 per cent of cases with sufficient data had auricular fibrillation 34 per cent had right heart failure 10 out of 16 roentgenographed cases had cardio thoracic indices over 55 and 35 patients had been treated with digitalis before embolism developed 18 patients (?4 per cent) died in the first attack and 9 died of subsequent em

bolism 23 out of 57 patients who survived the first attack had recurrences Only one fifth survived 10 years after past embolism 6 out of 14 survivors had severe persistent sequelae (hemiplegia)

Of the 194 *females* of the series 125 (65 per cent) had been *pregnant* and 109 (56 per cent) had given *birth* to 1 or more liveborn children Abortion was induced in 29 cases 4 patients (3 2 per cent) died during pregnancy or puerperium though death was not attributable only to the pregnancy in all cases Persistent aggravation of the heart disease after pregnancy was mentioned in one fourth of the cases chiefly patients with preceding heart trouble Three fourths of all pregnant females had had one or more pregnancies without persistent aggravation of the heart disease

The arterial blood pressure in isolated mitral stenosis in the present series showed a rise with advancing age This is in accord with the findings in other series of cases of mitral stenosis and did not definitely exceed the findings by other authors in average populations Arterial hypertension was a characteristic feature of the course of the disease in only few cases

The frequency of complicating disorders was not higher than would be expected by mere coincidence

The survival during the period of observation for the whole series of females was 40 per cent after 10 years and 18 per cent after 20 years for the whole series of males it was 29 per cent after 10 years and 8 per cent after 18 years Either sex showed a decidedly lower survival than similar groups in the average population

As a result of the survival analyses starting at the time of the first examination four prognostic groups were established These may be briefly mentioned

Group A – Patients in Class II with sinus rhythm The median survival time is many years (over 20 years)

Group B – Patients in Class III with sinus rhythm The median survival time was found to be from 7 to 8 years for females and from 5 to 6 years in the case of males

Group C – Patient with auricular fibrillation in Classes II and III The median survival time is exactly the same as that of Group B even though patients of Group C were from 6 to 10 years older

Group D Patients in *Class IV* The median survival time is under 1 year

It was found in Groups B and C that a negative T_3 and an iso electric T_1 (with or without other T wave anomalies) tended to give a somewhat graver prognosis than did normal T waves Furthermore right axis deviation in Group B had a tendency to give a poorer prognosis than that found in the absence of right axis deviation

Otherwise other clinical findings (cardiac asthma acute pulmonary oedema pulmonary emboli and arterial emboli) did not in the separate groups show definite tendencies to give a prognosis that was worse than that found in the absence of these symptoms

Chapter V

Twenty one cases with not verified but *clinically probable mitral stenosis* showed a close conformity with the cases of diagnosed isolated mitral stenosis this applies to all essential points in the course of the disease to the nature and frequency of complications and to the duration of life

Chapter VI

Fifty nine cases of *mitral stenosis combined with aortic valvular disease* are dealt with on the same lines as the cases of isolated mitral stenosis

The group comprised 28 males and 31 females the average age was 47 5 years at the *first examination* 72 per cent had had rheumatic fever The average age when the first symptom developed was 31 2 years and the average duration of the symptoms at the first observation was 11 3 years 47 per cent had auricular fibrillation 25 per cent had right heart failure 46 out of 53 patients had cardio thoracic indices over 50 16 patients were in Class II 29 in Class III and 14 in Class IV

Five patients had right axis deviation 43 had a normal QRS axis and 11 had left axis deviation 26 patients had normal T waves 5 had a negative T_3 1 had negative T and T_3 17 had an iso electric T_1 and 10 had a negative T_1 Bundle branch block was observed in 2 cases

Thirteen out of 16 patients roentgenographed in the right anterior oblique position showed enlargement of the left atrium Enlargement of the left ventricle was found in 35 out of 53 patients examined

Forty seven patients (80 per cent) *died during the period of observation* The average age at death was 48 4 years With regard to causes of death and findings at autopsy this group is in almost complete accord with that of isolated mitral stenosis It may however be mentioned that one fifth of autopsied cases of mitral and aortic valvular disease had tricuspid stenosis

Twelve *surviving* patients at an average age of 43 6 years at the time of the follow up presented few signs of progression of the heart disease after a period of observation averaging 8 7 years

Most cases of mitral stenosis with aortic valvular disease showed an earlier and more frequent initial *rheumatic infection* than did cases of isolated mitral stenosis

With regard to the *course of the disease complications* and *survival times* after the first rheumatic infection and after the onset of the first heart symptom cases of mitral and aortic valvular disease do not differ essentially from those of isolated mitral stenosis even though the former showed a tendency to a shorter survival time after auricular fibrillation or right heart failure had been ascertained

Notes in Conclusion

The pronounced tendency to progression of the heart disease in the whole series is stressed and on this basis the timeliness of surgical operation of mitral stenosis is discussed

Dansk resume

INDLEDNING

Formålet med dette arbejde er at give et nyt bidrag til beskrivelsen af mitral stenosens forløb og prognose

KAPITEL 1

Der gives en kort oversigt over den historiske udvikling af vort kendskab til mitralstenosen med særligt henblik på sygdommens diagnose og patologi

KAPITEL 2

Hovedtrækkene i de tidligere undersøgelser over mitralstenosens prognose gennemgås Den eneste større systematiske undersøgelse er foretaget af *Grant* der fulgte sit soldatermateriale igennem 10 år Hans materiale omfatter kun mænd og væsentlig aldersklasserne mellem 20 og 40 år Ved efterundersøgelsen var ca 1/3 døde 1/3 forværrede og 1/3 uforandrede Det påpeges slutteligt at systematiske studier over forløbet af mitralstenosen i de ældre dekader mangler i litteraturen

KAPITEL 3

Egne undersøgelser omfatter en klinisk analyse af forløbet hos 351 patienter med mitralstenose der første gang er undersøgt i årene 1933–49 og eftersporet i 1951–53 således at observationstiden efter første undersøgelse varierer mellem 3 og 20 år Materialet deles efter angivne kriterier i 3 hovedgrupper 271 patienter med isoleret mitralstenose 21 patienter med klinisk sandsynlig mitral stenose og 59 patienter med mitralstenose kombineret med aortafejl Materialet er samlet fra 2 kilder 285 patienter fra Rigshospitalets medicinske afdeling *B* og 66 patienter fra professor dr med *Erik Warburgs* privatpraksis

I observationstiden er 257 patienter døde og 94 lever ved efterundersøgelsen Bortset fra en enkelt emigreret patient er det lykkedes at opspore alle patienter ved den endelige opgørelse Det er lykkedes at indsamle fyldige oplysninger om sygdomsforløbet hos flertallet af de i observationstiden døde patienter og 90 af 94 overlevende patienter er efterundersøgt af forfatteren Også hos de 4

ikke efterundersøgte er tilstanden ved tidspunktet for efterundersøgelsen blevet oplyst.

I kapitlet gennemgås videre kriterierne for de kliniske diagnoser og sikkerheden af disse bedømt ved autopsifund og fundene ved efterundersøgelsen og de anvendte røntgenologiske elektrokardiografiske og kliniske kriterier omtales

Sluttelig omtales de i vurderingen af prognosen anvendte principper der bygger på en samlet vurdering af overlevelsen efter bestemte tidsrum med henstyntagen til såvel de overlevende som de i observationstiden døde patienter. Man anvender den indirekte (eller aktuariske) metode til beregning af overlevelsen. Overlevelsestiderne er dels angivet som de aritmetiske gennemsnit for døde og for levende hver for sig og dels udtrykt ved den mediane overlevelsestid der angiver det tidsrum i hvilket 50 % af patienterne er døde

Kapitel 4

Kapitlet giver en udførlig gennemgang af det kliniske billede og det samlede sygdomsforløb hos 271 patienter med isoleret mitralstenose

Materialet omfatter 194 kvinder og 77 mænd med gennemsnitsalderen 41 6 år ved første observation Hovedparten af patienterne er mellem 30 og 49 år og 96 % er over 50 år 59 % har haft rheumatisk infektion gennemsnitsalderen ved den rheumatiske initialinfektion var 15 4 år og gennemsnitsintervallet mellem initialinfektionen og første observation var 25 1 år Gennemsnitsalderen ved første hjertesymptom var 31 2 år og gennemsnitsvarigheden af symptomerne ved første observation var 10 3 år 57 % af patienterne havde arytmia perpetua og 25 % højresidig hjerteinsufficiens Hjertestørrelsen udtrykt ved den cardiothoracale index viser meget betydelige variationer således at 158 af 181 kvinder og 51 af 69 mænd har cardiothoracal index over 50 og adskillige af disse over 65 En analyse viser at arytmia perpetua næsten altid ledsages af cardiothoracal index over 50 og hyppigst over 55 og ved højresidig hjerteinsufficiens finder man i 80 % af tilfældene arytmia perpetua og næsten altid cardiothoracal index over 55

Ved første observation klassificeredes 21 % af patienterne i funktionsgruppe II 59 % i funktionsgruppe III og 20 % i funktionsgruppe IV Ved sammenligning mellem inddeling efter funktionskapacitet og inddeling efter hjerterytme hjerte størrelse og tegn på højresidig hjerteinsufficiens viser det sig at patienter i funktionsgruppe II overvejende har sinusrytme lavere grader af cardiothoracal index og manglende tegn på højresidig hjerteinsufficiens medens patienter i funktionsgruppe IV næsten alle har arytmia perpetua højere cardiothoracal index og viser tegn på højresidig hjerteinsufficiens Patienter i funktionsgruppe III ligger midt imellem

Røntgenundersøgelsen har ved påvisning af forstørret venstre atrium eller ved fundet af en lige venstre hjertekontur eventuelt med prominens af anden venstre bue kunnet støtte den kliniske diagnose i næsten alle de velundersøgte tilfælde

Hos 269 patienter foreligger elektrokardiogram optaget i de 3 standard afledninger Hos 34 af 114 patienter med sinusrytme forekom abnorme P takker 29 % havde højresidig axedeviation og 3 % venstresidig axedeviation Abnorme T takker var hyppige og forekom navnlig ved arytmia perpetua Grenblok forekom hos 5 patienter og low voltage hos 2 patienter T takforandringerne forekom i det overvejende antal af tilfældene i funktionsgruppe III og IV

Ved efterundersøgelsen efter 3–20 år gennemsnitligt 12 ar var 189 patienter døde (70 %) Gennemsnitsalderen ved død var 47 0 år og 42 % var døde efter det 50 år Dødsårsagerne var hos 62 % hjerteinsufficiens 22 % thromboembolliske komplikationer 9 % infektioner og 8 % var døde af andre årsager Kun 3 patienter er døde af sikkert rheumatisk recidiv og 4 andre kan muligvis være døde heraf 4 patienter døde af subakut bakteriel endokarditis 9 døde i akut lungeødem Hos 85 af de 189 døde er der foretaget autopsi I 5 tilfælde (6 %) fandtes en trikuspidalstenose i 6 tilfælde symfysis pericardii i 27 tilfælde forkalkning i mitralklapperne og i 33 tilfælde fandtes atheromatose eller arteriosclerose i coronararterierne

Af 82 overlevende er 78 efterundersøgt med en gennemsnitlig observationstid pa 9 7 år Gennemsnitsalderen ved efterundersøgelsen var 49 1 år 69 % havde arytmia perpetua og 42 % højresidig hjerteinsufficiens Hos 40 af 41 røntgenundersøgte patienter (56 %) var den cardiothoracale index vokset med mere end 10 % og i 34 af 78 tilfælde (44 %) blev patienten ved efterundersøgelsen placeret i en ringere funktionsgruppe end ved første undersøgelse Ialt viste mere end /3 af de efterundersøgte patienter efter de ovennævnte kriterier tegn på progression af hjertelidelsen i observationstiden

Hos 1 af de 4 ikke efterundersøgte patienter foreligger der oplysninger om sikker progression af hjertelidelsen

Der gives en udførlig gennemgang af den rheumatiske initialinfektion o antallet af de rheumatiske recidiver i relation til det senere sygdomsforløb og man konkluderer at antallet af rheumatiske recidiver ikke i eget materiale har haft nogen sikker indflydelse på overlevelsestiden efter initialinfektionen En tidlig initialinfektion har givet en lavere gennemsnitsalder end en sen initial infektion Overlevelsestiderne efter initialinfektionen har været gennemsnitligt 30 1 år for de døde og 33 3 år for de overlevende

Den gennemsnitlige overlevelsestid efter begyndelsen af hjertesymptomerne er fundet til 14 3 år for 181 døde og 20 5 år for 86 overlevende patienter Over levelsestiden har varieret fra 1 år til 52 år efter første symptom Det frem hæves at 31 af 189 døde er døde inden 5 år efter symptomernes begyndelse Den gennemsnitlige overlevelsestid efter hjertesymptomernes begyndelse er fundet aftagende med stigende alder ved første symptom således som man måtte vente det

Arytmia perpetua er verificeret hos 84 % af de i observationstiden døde patienter med oplyst hjerterytme og hos 70 % af de overlevende Gennemsnits alderen ved konstateringen af arytmia perpetua har været 43 8 år og arytmien er gennemsnitligt først konstateret 27 år efter den rheumatiske initialinfektion og 10 6 år efter første hjertesymptom 43 % af patienterne havde højresidig hjerteinsufficiens ved konstateringen af arytmien Af kvinderne levede 32 % 10 år efter konstateret arytmi og af mændene levede 21 % efter dette tidsrum Efter påvist arytmi var af kvinderne 50 % døde efter 6–7 år og af mændene 50 % døde efter 4–5 år Ialt 18 af 271 patienter har haft paroxystisk arytmia perpetua der hos 16 patienter gik over i kronisk arytmi Paroxystisk takykardi er fundet hos 5 patienter (5 % af gruppen med sinusrytme)

Objektivt konstateret højresidig hjerteinsufficiens er fundet hos 81 % af de døde mitralstenoser og i 68 % af hele materialet Gennemsnitsalderen ved kon stateret højresidig hjerteinsufficiens var 45 6 år Gennemsnitsintervallet fra første rheumatiske infektion er 29 år og efter første hjertesymptom 13 2 år Den højresidige hjerteinsufficiens var i 75 % af tilfældene ledsaget af arytmia per petua Efter konstateret højresidig hjerteinsufficiens var 50 % døde efter 2 3 år men det fremhæves at en gruppe på 11 % har levet 10 år eller mere med højresidig hjerteinsufficiens For patienter med sinusrytme var overlevelses tiden efter påvist højresidig hjerteinsufficiens tydeligt kortere end for hele gruppen

Asthma cardiale akut lungeødem er beskrevet hos 45 af 271 patienter (17 %) Gennemsnitsalderen var 37 4 år ved første attak 6 patienter døde i første an fald og 3 døde i et recidiv Af patienter som overstod første anfald overlevede 58 % i 5 år og 37 % i 10 år Af patienter under 50 år overlevede 46 % i 10 år Risikoen for død i akut lungeødem er beregnet til 3 % for hele materialet og til 8 % for patienter med overstået første anfald Patienterne i denne gruppe har haft en lavere gennemsnitsalder ved død eller efterundersøgelse end total materialet og asthma cardiale–akut lungeødem har således været ledsagesymp tomer ved en tidligt symptomgivende form for mitral tenosen der med hensyn til opnået levealder har haft en noget dårligere prognose end gennemsnittet i materialet

Hæmoptyser der ikke har været ledsagesymptomer ved asthma cardiale akut lungeødem eller lungeinfarkt er forekommet i 31 tilfælde med gennemsnits alderen 29 2 år ved første attak Overlevelsen efter første anfald af hæmoptyse er fundet til 46 % efter 10 års forløb og synes at være lavere ved gentagne hæmoptyser Hæmoptyserne har ligesom asthma cardiale-akut lungeødem været ledsagesymptomer ved tidligt symptomgivende mitralstenoser der med hensyn til opnået alder har været mindre gunstigt stillet end gennemsnittet af mitralstenoser men det fremhæves at der ikke i eget materiale er forekommet dødsfald af hæmoptyser

Lungeinfarkter er forekommet hos 55 patienter (20 % af materialet) og hos 50 af 189 døde patienter (27 %) Komplikationen har hyppigst ramt patienter med arytmia perpetua højresidig hjerteinsufficiens og høj cardiothoracal index Gennemsnitsalderen ved lungeinfarkt var 45 1 år Af klinisk diagnosticerede tilfælde døde 44 % i tilslutning til første lungeinfarkt Af de overlevende fik ½ recidiver og kun ¼ var i live efter 10 års forløb

Pneumonier er beskrevet hos 97 patienter (36 %)

Hæmosiderose i lungerne er kun sikkert påvist hos 1 af 197 røntgenundersøgte patienter

Arterielle embolier i det store kredsløb er set hos 75 patienter (28 %) og hos 61 af 189 døde (32 %) Gennemsnitsalderen ved første emboli var 45 2 år 85 % af sikkert oplyste tilfælde havde arytmia perpetua 34 % højresidig hjerteinsufficiens 10 af 16 røntgenundersøgte havde cardiothoracal index over 55 og 35 patienter (24 %) døde i første attak og 9 døde af senere emboli Recidiver forekom hos 28 af 57 patienter som overlevede første emboli Kun ⅓ levede 10 år efter overstaet emboli 6 af 11 overlevende patienter med tidligere emboli havde svære blivende følger (hemiplegi)

Af materialets 194 kvinder har 125 (65 %) været gravide og 109 kvinder (56 %) har født 1 eller flere levende børn Abortus provocatus er foretaget i 29 tilfælde 4 patienter er døde under graviditet eller i puerperium (3 %) men ikke alle disse dødsfald kan alene tilskrives graviditeten Blivende forværring af hjertelidelsen efter graviditet er angivet i ¼ af tilfældene fortrinsvis blandt patienter med forudgående hjertebesvær ¾ af de gravide har gennemgået 1 eller flere graviditeter uden blivende forværring af hjertelidelsen

Det arterielle blodtryk ved isoleret mitralstenose viser i eget materiale en stigning med alderen der svarer til hvad man finder i andre materialer af

mitralstenoser og hvad andre undersøgere har fundet i gennemsnitsbefolkningen Kun i enkelte tilfælde har den arterielle hypertensionssygdom præget sygdomsforløbet

Komplicerende sygdomme er ikke set med større frekvens end man kan vente ved tilfældigt sammentræf

Overlevelsen i observationstiden er for det samlede materiale af kvinder 40 % efter 10 år og 18 % efter 20 år og for mændene 29 % efter 10 år og 8 % efter 18 år Begge køn viser en udtalt lavere overlevelse end tilsvarende grupper i gennemsnitsbefolkningen

Som resultat af de foretagne overlevelsesanalyser der starter ved tidspunktet for første observation har man opstillet prognosegrupper der kort skal omtales

Gruppe A Patienter i funktionsgruppe II med sinusrytme Den mediane overlevelsestid er mange år (over 20 år)

Gruppe B Patienter i funktionsgruppe III med sinusrytme Den mediane overlevelsestid er for kvinder fundet til 7–8 år og for mænd 5–6 år

Gruppe C Patienter med arytmia perpetua i funktionsgruppe II og III Den mediane overlevelsestid er ganske den samme som for gruppe B selvom gruppe C er 6–10 år ældre

Gruppe D Patienter i funktion gruppe IV Den mediane overlevelsestid er under 1 år

Inden for prognosegrupperne B og C er der fundet en tendens til at negativ T_3 og isoelektrisk T_1 (med eller uden andre T anomalier) giver en lidt dårligere prognose end normale T takker Endvidere har højresidig axedeviation i gruppe B vist en tendens til dårligere prognose end manglende højresidig axedeviation

Iøvrigt har andre kliniske fund (asthma cardiale akut lungeødem lungeembolier og arterielle embolier) ikke inden for de enkelte grupper vist sikre tendenser til en dårligere prognose end mangel på dette fund

Kapitel 5

21 patienter med ikke verificeret men klinisk sandsynlig mitralstenose viser på alle væsentlige punkter i sygdomsforløbet i arten og hyppigheden af komplikationerne og i opnået levealder en nær overensstemmelse med de isolerede mitralstenoser

59 patienter med mitralstenose kombineret med aortafejl gennemgås efter samme retningslinier som de isolerede mitralstenoser Der er 28 mænd og 31 kvinder og gennemsnitsalderen er 42 5 år ved første observation 72 % har haft gigtfeber

Gennemsnitsalderen ved første symptom er 31 2 år og gennemsnitsvarighe den af symptomerne ved første observation er 11 3 år 47 % har arytmia per petua og 25 % højresidig hjerteinsufficiens 46 af 53 patienter har cardiothoracal index over 50 16 patienter er i funktionsgruppe II 29 i funktionsgruppe III og 14 patienter i funktionsgruppe IV

5 patienter har højresidig axedeviation 43 har normal QRS axe og 11 har venstresidig axedeviation 26 patienter havde normale T takker 5 havde negativ T_3 1 negativ T og T_3 17 havde isolektrisk T_1 og 10 havde negativ T_1 Grenblok forekom i 2 tilfælde

13 af 16 patienter der var røntgenundersøgte med optagelse i højre skrå diameter viste forstørret venstre atrium Forstørret venstre ventrikel fandtes hos 35 af 53 undersøgte patienter

I observationstiden var 47 patienter døde (80 %) Gennemsnitsalderen ved død var 48 4 ar Med hensyn til dødsårsager og autopsifund slutter materialet sig meget nært til de isolerede mitralstenoser Kun skal det fremhæves at ⅓ af de secerede mitralaortafejl havde trikuspidalstenose

12 overlevende patienter med gennemsnitsalderen 43 6 år ved efterundersøgelsen frembød få tegn på progression af hjertelidelsen efter en gennemsnitlig observationstid på 8 7 ar

Mitralstenose kombineret med aortafejl viser gennemgående en tidligere og hyppigere initial rheumatisk infektion end de isolerede mitralstenoser

Mitralstenoser med aortafejl adskiller sig med hensyn til sygdomsforløb komplikationer og overlevelsestider efter første rheumatiske infektion og efter første hjertesymptom ikke væsentligt fra de isolerede mitralstenoser men der er fundet en tendens til kortere overlevelsestid efter konstateret arytmia perpetua og højresidig hjerteinsufficiens for mitralstenoser med aortafejl

AFSLUTTENDE BEMÆRKNINGER

Den stærke tendens til progression af hjertelidelsen i hele materialet fremhæves og på denne baggrund diskuteres betimeligheden af operativ behandling af mitralstenose

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